

AMERICAN JOURNAL OF OPHTHALMOLOGY

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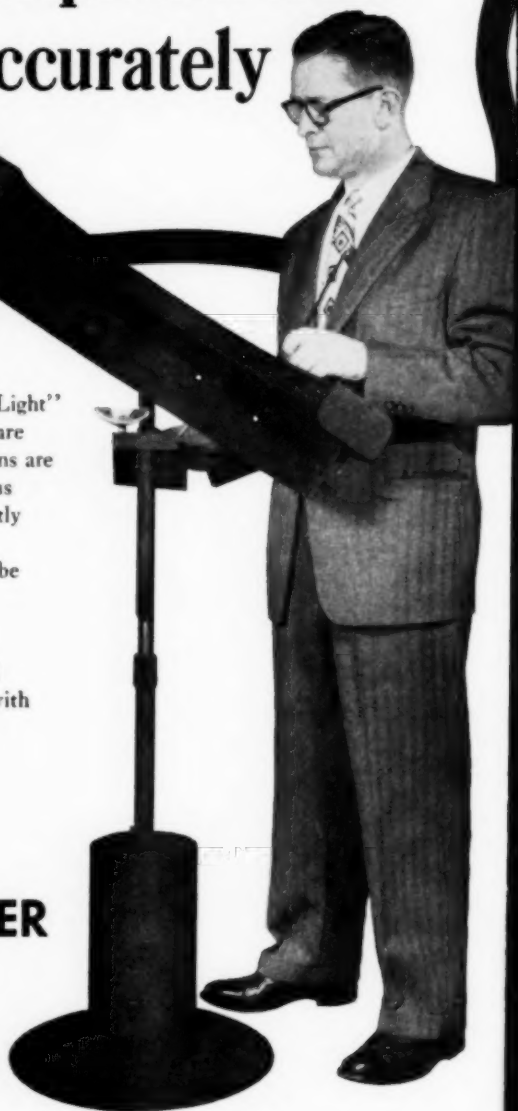
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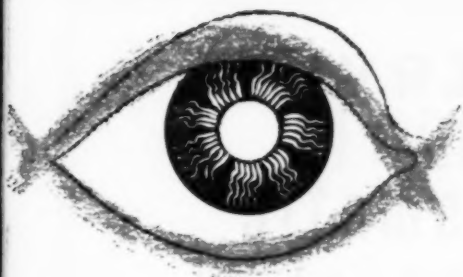
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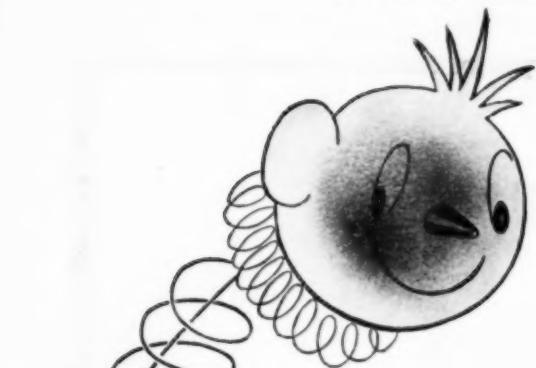
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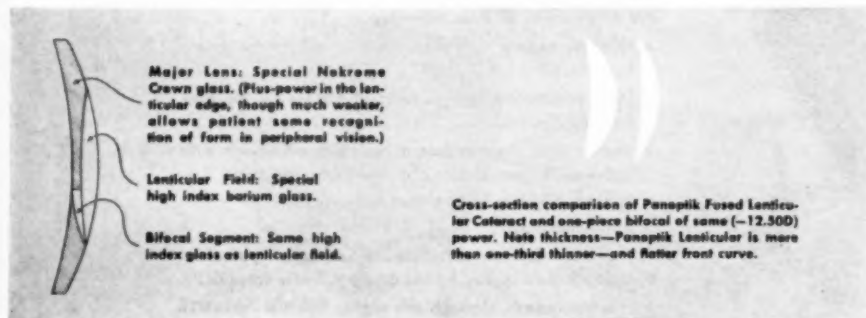
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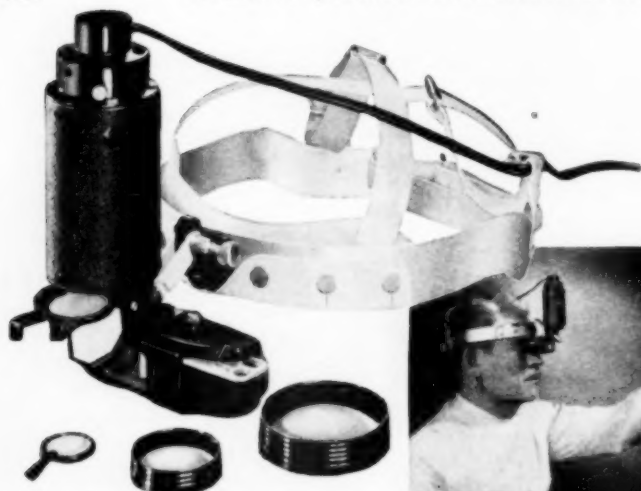
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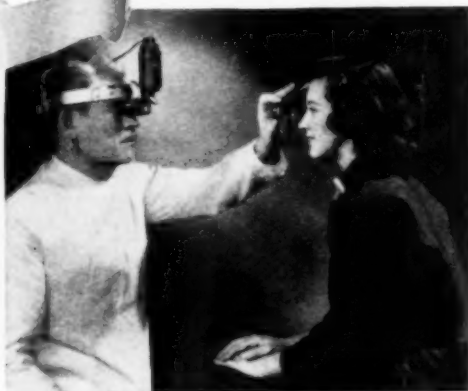
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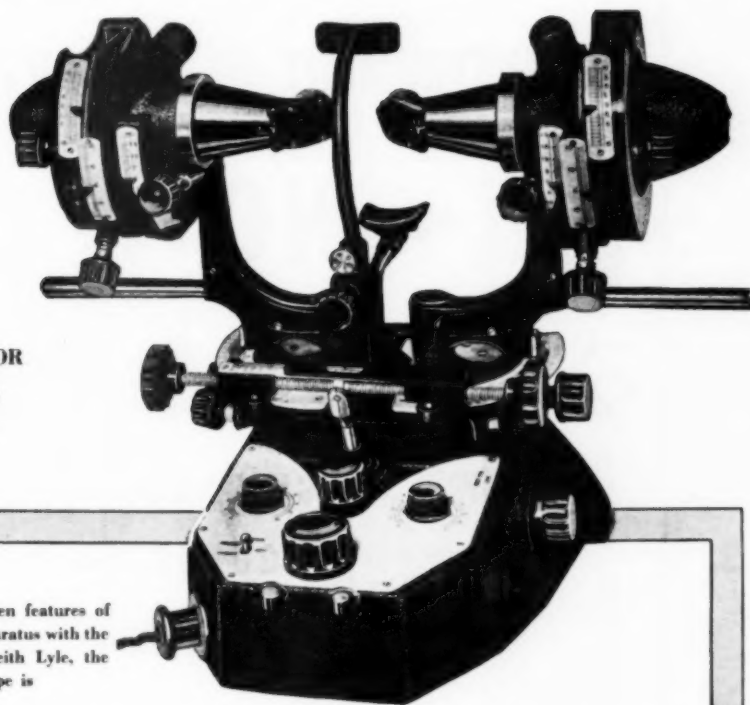


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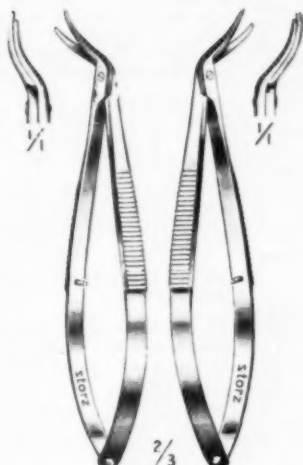
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J. Graham, R. Co., and Leopold, I. H.: Arch. of Ophth. 69:38 (Jan.) 1955
J. Graham, I. H.: Am. J. Ophth. (Jan.) 1955
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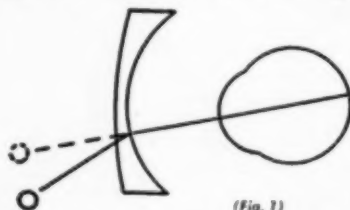
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It is an established fact that myopes have a lot of trouble becoming adjusted to bifocals. Hyperopes usually have very little trouble, and people wearing cataract bifocals no trouble at all, if the lenses are well designed and if the segments are properly placed.

The reason that myopic bifocals are troublesome lies in the fact that through the segments, even of the best available bifocals, base down prism



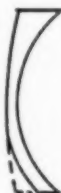
(Fig. 1)

is encountered. This base down prism makes objects appear farther away and higher than they really are. See figure 1.

The myope, before bifocals fixed his line of vision through a point 8 mm. below the distance center, invariably tipped his head and looked through a point near the distance center, thus avoiding prismatic effect. The hyperope on the other hand is not troubled by the base up prism

he encounters and has little or no difficulty with bifocals.

From the foregoing it would seem that if the base down prism found in the segments of myopic bifocals could be neutralized, the problem would be solved. We have found this to be true. We have also found that the only practical way to accomplish this neutralization is by "slabbing off" the proper amount from the bifocal segments. See figure 2.



(Fig. 2)

If we take a case requiring O.U. -6.00 with a +2.00 add made up in a small segment bifocal, we would "slab off" 4.8 degrees of prism base up from both segments. ($6 \times .8 = 4.8$) that is, the distance correction through the 90th meridian times .8, the distance in cms. from distance center to reading point, equals the amount of base down prism that must be neutralized.

A case requiring O.D. -5.00 and O.S. -7.00 would have a 4 degree prism base up slab off on the right and a 5.6 degree prism base up slab off on the left lens.

In this case, two things would have been accomplished: the annoying base down prism would have been neutralized and the induced vertical imbalance corrected.

"IF IT'S A LENS PROBLEM, LET'S LOOK AT IT TOGETHER"

AMERICAN JOURNAL OF OPHTHALMOLOGY

SERIES 3 • VOLUME 36 • NUMBER 10 • OCTOBER, 1953

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ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, Heredity	1479
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A CLASSIFICATION OF RETROLENTAL FIBROPLASIA*

The advantages of adopting a uniform classification for retrolental fibroplasia are obvious. If ophthalmologists and pediatricians can agree on the designation of the successive stages, investigative efforts in the future can be based on uniform definitive diagnostic criteria. The adoption of the same classification by all workers in the field is particularly important now in view of the fact that there is afoot a nation-wide co-operative plan for the study of the causes of retrolental fibroplasia. Furthermore, an agreement on the stages of the disease is necessary in order to make comparable analyses not only of treatment at various localities but also of incidence figures. It is obvious that figures based on different diagnostic criteria cannot be compared.

A joint committee for the study of retro-

lental fibroplasia was appointed by the National Society for the Prevention of Blindness.

A subcommittee was appointed consisting of Dr. Algernon B. Reese, chairman; Dr. Merrill J. King and Dr. William C. Owens to submit a classification of retrolental fibroplasia. The classification herewith given was submitted and adopted by the parent committee. The subcommittee was then asked to document each of the stages with a suitable illustration. The illustrations herewith given were submitted and adopted as exemplifying adequately the various stages.

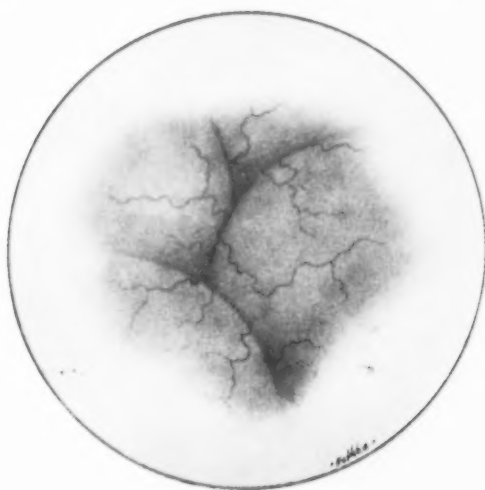
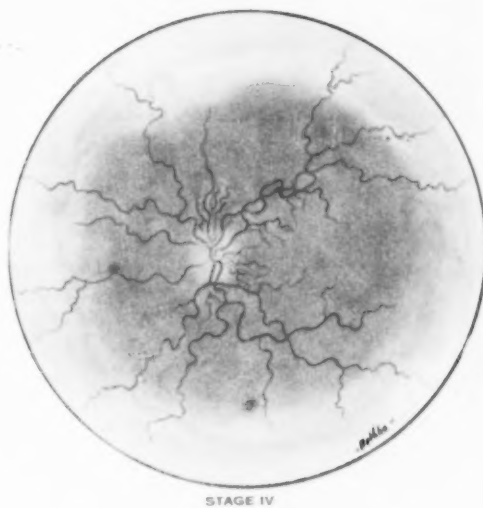
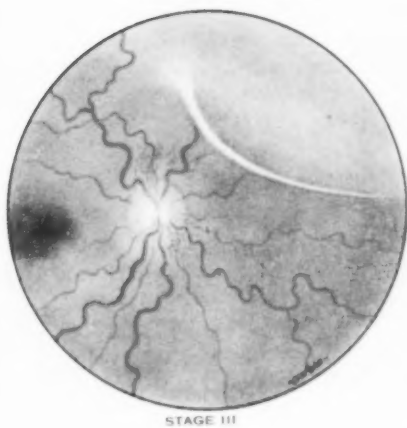
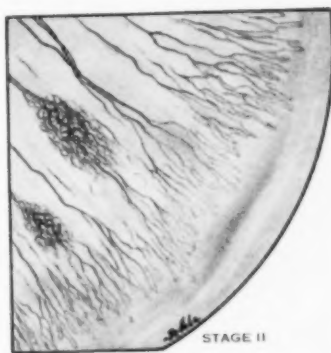
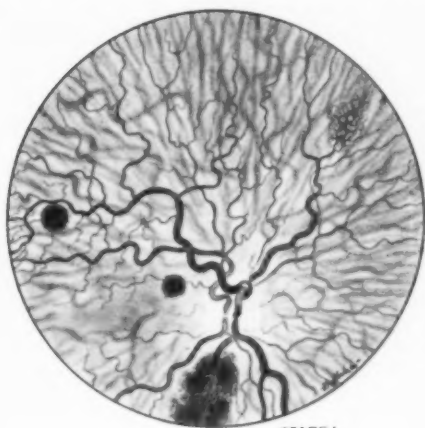
Eyes that have advanced to Grade V of the cicatricial stage sometimes show corneal opacifications, posterior synechias, iris atrophy, pupillary membrane, and occasionally cataract. Also they may show secondary glaucoma and buphthalmos. All of these later sequelae occur in the Grade-V stage and are therefore properly classified as such.

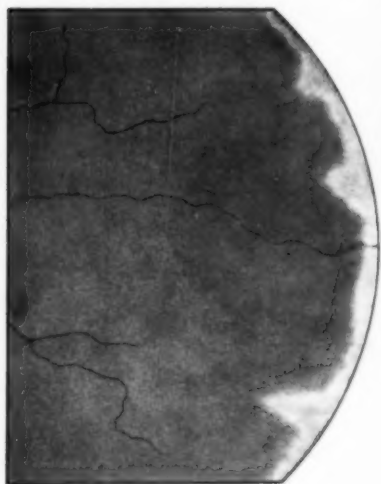
* This work was supported by the Dunlevy Milbank Foundation.

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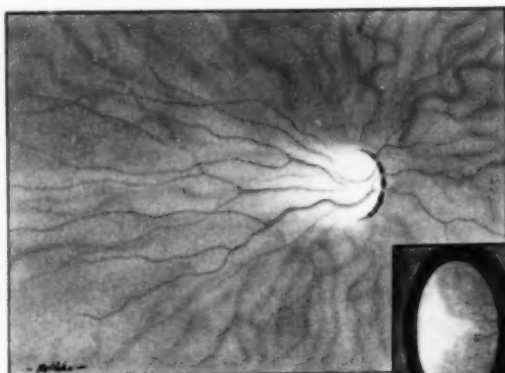
STAGES OF RETROLENTAL FIBROPLASIA IN THE
ACTIVE PHASE

- I. *Dilatation and tortuosity of retinal vessels*
Hemorrhages may or may not be present
Early neovascularization especially in the extreme periphery of the visible fundus may be present
- II. *Stage I plus neovascularization and some peripheral retinal clouding*
Hemorrhages are usually present
Vitreous clouding may or may not be present
Spontaneous regression may occur
- III. *Stage II plus retinal detachment in the periphery of the fundus*
Spontaneous regression unlikely
- IV. *Hemispheric or circumferential retinal detachment*
Elevation of the retina over a large area, but still with some retina in position
- V. *Complete retinal detachment*

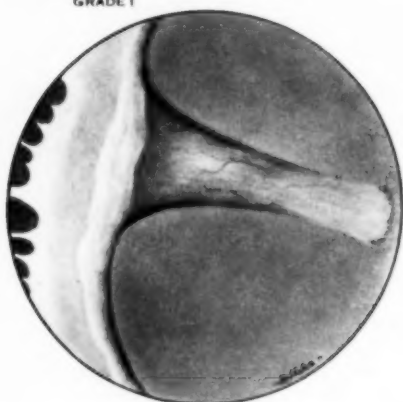




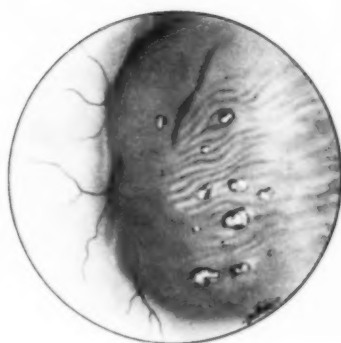
GRADE I



GRADE II



GRADE III



GRADE IV



GRADE V





GRADES OF RETROLENTAL FIBROPLASIA IN THE CICATRICIAL PHASE

- I. *Small mass of opaque tissue in periphery of the fundus without visible retinal detachment*
The fundus may have a pale appearance
The blood vessels may be attenuated
- II. *Larger mass of opaque tissue in periphery of the fundus with some localized retinal detachment*
The disc is distorted by traction toward the side of the tissue, which is usually temporally
Cases ending in Grade I or II have useful vision
- III. *Larger mass of opaque tissue in periphery incorporating a retinal fold which extends to the disc*
Visual acuity varies from 5/200 to 20/50
- IV. *Retrolental tissue covering part of pupillary area*
Small area of attached retina may still be visible or only a red reflex over a sector of the fundus may be seen
- V. *Retrolental tissue covering entire pupillary area*
No fundus reflex present

RETROLENTAL FIBROPLASIA AND RELATED OCULAR DISEASES*

CLASSIFICATION, ETIOLOGY, AND PROPHYLAXIS

THADDEUS S. SZEWCZYK, M.D.

East Saint Louis, Illinois

It is becoming increasingly apparent from current reports in the literature that oxygen may be the responsible factor in the causation of retrolental fibroplasia.

Ryan reported that no case of retrolental fibroplasia had occurred at the Women's Hospital in Melbourne, Australia, until it became a practice to administer oxygen liberally to all babies even when they apparently did not require it. During this time, 21 cases of retrolental fibroplasia developed. When the use of oxygen was restricted to those babies that were actually cyanosed, no further cases of this disease developed.

Ryan postulated that oxygen may act as a toxic agent, stimulate mitosis, overgrowth of glial and fibrous tissue, increase the vascularity, increase the growth of the inner layer of the optic cup, and lead to further detachment of the normally loosely coapted inner and outer layers of the retina.

Patz, Hoeck, and De La Cruz report a study of 65 premature babies with a birth weight of under three and one-half pounds. Twenty-eight of the babies were kept in an oxygen environment of 65 to 70 percent from four to seven weeks, and 37 in an oxygen concentration under 40 percent for 24 hours to two weeks. The first group was weaned gradually from the high oxygen over a period of one week, while in the second group the weaning period was from one to three days.

Of the 28 babies who were kept in a high-oxygen concentration, five developed a total or almost complete permanent retinal

membrane behind the lens; two progressed to the stage of detachment of the retina, new vessel formation, retinal hemorrhages, and vitreous opacities; seven developed vascular changes, retinal edema, retinal hemorrhages, and vitreous clouding and opacities; and three developed marked dilatation and tortuosity of the retinal vessels with occasional areas of mild retinal edema.

Of the 37 babies kept in a low-oxygen environment only two progressed to the stage of retinal edema, vascular dilatation, retinal hemorrhages, and vitreous clouding and opacities; and four developed marked vascular dilatation and tortuosity of the retinal vessels with occasional areas of mild retinal edema.

These observations and the fact that they were unable to produce progressive changes in two babies when they were suddenly removed from an environment of high-oxygen concentration suggested to these authors that "prolonged high oxygen, if injurious, results from a direct effect instead of from relative anoxia that might result from the too rapid withdrawal from oxygen."

On superficial examination of these reports, it would indeed appear that oxygen is toxic and that its use does cause the eventual development of retrolental fibroplasia. As I will show later, however, the true cause of retrolental fibroplasia is hypoxia and this, in the greatest majority of the cases, is produced by improper use of oxygen and by its too rapid withdrawal from a child who has become acclimated to it.

Crosse and Evans, in a recent statistical study of this disease in England, reported that there was a direct relationship between the amount and duration of oxygen administration and the incidence of retrolental fibroplasia. When oxygen was used freely, the

* From the Department of Ophthalmology, Saint Louis University School of Medicine, and Premature Center, Christian Welfare Hospital, East Saint Louis, Illinois. This is the elaboration of the paper read before the Central Illinois Society of Ophthalmology and Otolaryngology, March 29, 1952.

incidence rose; when its use was restricted, no cases of retrolental fibroplasia developed. It was their opinion that changes in the retina in this disease derive from a preliminary adjustment of the retina to a high-oxygen tension whereby the retina loses its ability to accommodate itself to relative anoxia on removal to atmospheric oxygen, having acquired an inertia of response.

Jefferson, in a recent study, found a direct relationship between the incidence of retrolental fibroplasia and the method of oxygen administration. When little or no oxygen was used in the care of premature babies, the incidence was extremely low.

In December, 1949, when oxygen tents were introduced and used routinely for all infants under three pounds, three cases of retrolental fibroplasia occurred in this weight group during the following months. In November, 1950, when it was decided to nurse every infant in the unit in an oxygen tent, even those over three pounds began to develop the disease.

In March, 1951, when soft plastic covers were introduced for use in the Sorento-type cot, so that oxygen was used more efficiently and in high concentrations, the incidence of the disease rose to the point where 75 percent of all infants, up to and including those four pounds in weight, developed it.

In October, 1951, use of oxygen was reduced to a minimum, and its withdrawal was carefully graded. Since that time only one serious case and two relatively mild cases of retrolental fibroplasia have occurred.

Jefferson also reported dramatic improvement within 48 hours in six early cases of retrolental fibroplasia treated by administration of oxygen in high concentrations. Four of these were kept in a concentration of 80 percent for four weeks and then the oxygen was very gradually withdrawn. In three cases the retina remained normal after the babies were removed from oxygen. The fourth infant's subsequent course was not so satisfactory, perhaps because of the more

advanced changes, with a definite retinal detachment, which existed at the time of replacement in oxygen. Two of the six cases were still in oxygen at the time of the report.

Jefferson's observations led him to believe that acclimatizing a premature infant to oxygen in high concentrations makes him more susceptible to the disease if he is suddenly transferred to a normal atmosphere because there is a sudden reduction in the tension of oxygen available to his tissues, and that the initial changes of the disease will rapidly regress when the oxygen tension is restored (by replacing the infant in high-oxygen concentrations).

Recently I reported that dilatation and tortuosity of the retinal vessels, neovascularization with or without hemorrhages, retinal edema, and even retinal separation develop in the eyes of premature babies when they are subjected to a sudden significant lowering of the oxygen concentration in their environment; that these changes are progressive in a high percentage of cases; and that they are readily reversed in their early stages by the administration of oxygen.

These phenomena have been observed on many occasions. So consistently, in fact, are the changes precursory to retrolental fibroplasia seen when there is some interference with oxygenation or the blood oxygen-carrying capacity (anemia) in a premature baby that I believe that retrolental fibroplasia can be produced in premature infants, regardless of birth weight, and even in full-term babies, simply by subjecting them to one or more episodes of sudden prolonged hypoxia.

I also stated that retrolental fibroplasia is preventable by the proper administration of oxygen; that prematures should be given minimal amounts of oxygen—just sufficient to meet their needs—and be weaned slowly; that excessive oxygen concentrations should be avoided.

In mid-September, 1951, the use of oxygen at the Christian Welfare Hospital was

restricted to babies under four-pounds birth weight. Whenever possible, low concentrations were used (under 45 percent). Shortly afterward, more and more babies in the very low weight group (two to four pounds), who were apparently in good condition when admitted, were cared for without the use of any supplemental oxygen. Whenever an infant developed fundus changes of a progressive nature (early retrolental fibroplasia), he was either placed back into an oxygen-enriched atmosphere or the oxygen concentration was increased, if he were still in an incubator.

During the following seven months, 147 surviving premature babies under five pounds of weight were cared for and discharged.

Of this number, one child developed a typical retrolental mass in one eye and a peripheral retinal fold with granular pigmentation of the rest of the fundus in the other eye; two children developed a retinal fold extending to the midperiphery in one eye, the other eye remained ophthalmoscopically normal except for some pigmentary disturbance; one child developed a peripheral retinal fold in one eye, the other remaining ophthalmoscopically normal; and one child was discharged with white areas in the extreme temporal periphery of both eyes but with otherwise normal-appearing eyes.

One hundred forty-two babies were discharged with normal eyes and have, in most instances, been re-examined on several occasions after discharge. We know of no child of this group who has developed any permanent ocular change after discharge from our nursery.

All of the five babies who had residual ocular defects were from the group attended in late 1951 and I believe that in all five any ocular damage could have been prevented if we had been more familiar with the proper treatment. The one child who developed retrolental fibroplasia in one eye and a retinal fold in the other eye progressed to this unhappy termination not because of

improper oxygen administration but because of our ignorance at the time of the harmful effect of transfusions when the retinovascular damage of hypoxia was present.

Of the remaining four babies, two developed severe upper respiratory infections while in incubators with relatively low concentrations of oxygen and the concentration was not raised sufficiently to meet the demands of the babies; and two, who had been subjected to several hypoxic episodes while in the incubators, were not weaned gradually enough from an oxygen-enriched atmosphere.

During the first four months of 1952, the policy of minimal use of oxygen and gradual weaning was well followed. During this time, only three infants out of a total of 74 surviving prematures developed funduscopic changes severe enough to require treatment. All three were successfully treated with oxygen, weaned, and discharged with normal fundi.

During the following four months, oxygen was again used freely and in high concentrations. In many instances babies were removed from oxygen without weaning.

Of 85 prematures who survived during this period of time, 17 developed fundus changes severe enough to require treatment. (One baby of this group had severe funduscopic changes on admission, which regressed spontaneously only to re-appear in a much more severe form several weeks after being discharged during an illness.)

Of this number, three babies developed severe retrolental fibroplasia with total loss of vision in both eyes, and two suffered loss of vision in one eye. The rest, after prolonged treatment with oxygen, were discharged with either normal fundi or minor defects compatible with good vision.

The fact that three infants lost the vision in both eyes and two in one eye, in spite of treatment with oxygen, might lead one to the conclusion that oxygen therapy for retrolental fibroplasia is no more successful than previously proposed and discarded methods.

Statistics, however, can lead one completely astray if the circumstances of individual variations are not taken into account.

Two of the infants, who developed bilateral retrolental fibroplasia, developed the early changes leading to this disease during my absence from the nursery. One had been out of an oxygen-enriched atmosphere for three weeks, and the other for four weeks. Both had very severe fundus changes at the time treatment was started and were probably in the irreversible stage.

In the other three, treatment was started shortly after the appearance of the fundus changes. The response to this treatment was as previously described—a marked improvement in a short time and gradual regression.

In two of these children, the fundi reverted to normal and the weaning process was begun. When the oxygen concentration had been reduced to about 45 percent, both suddenly showed marked vitreous hemorrhages and marked vascular and retinal changes.

Previous experience leads one to suspect immediately that the constant oxygen supply to the babies had in some way been interrupted. On investigation, it was found that to attain a lowered concentration in the incubators it had been necessary to turn the oxygen-flow valves to two liters per minute. These valves, while they functioned efficiently when set at four or more liters, were very erratic at lower settings and could then be made to turn off completely simply by tapping the adjusting handle. The valves were replaced, and the oxygen concentration increased.

In spite of prolonged treatment, complete organization of the vitreous and retinal detachment took place in both eyes of one infant and in one eye of the other. (The fellow eye developed a thin retrolental membrane through which the fundus could clearly be visualized. No detachment could be seen but the disc was distorted and the pigmentation scant and granular. The eye was highly myopic.)

The third child was similarly injured by a sudden decrease of available oxygen during treatment on at least two occasions: once when a small defect in the lip of the mason filtering jar allowed escape of oxygen into the nursery rather than into the incubator, and again when a faulty rubber gasket allowed a similar leakage. In both instances this was not discovered till the oxygen concentration was measured with an oximeter and found to be at room level.

Since September, 1952, it has again become our policy to administer oxygen only to those prematures who seemed to require it, to keep the concentration low except when otherwise indicated, and to wean off slowly those babies who had become acclimatized to an enriched atmosphere.

The incidence of retrolental fibroplasia immediately fell and there was no difficulty with this condition until December when an epidemic of "influenza" struck this area and three premature babies developed severe upper respiratory infections. All three developed very severe fundus changes, were treated with oxygen, but showed only transient improvement and progressed to total loss of vision in both eyes.

In all three children the respiratory infection did not respond to any treatment, lasted for several weeks, and then was followed by a reinfection in two, complicated by an otitis media in one child and a fibrocystic pancreas and severe anemia in the other.

For weeks their nasal passages were so blocked by secretions that frequent removal by suction was necessary and all three had frequent attacks of cyanosis even though kept in a very highly concentrated atmosphere (oxygen concentration 90+ percent). It is almost certain that the respiratory embarrassment kept these children in a hypoxic state even though oxygen in high concentration was available to them.

During this same four month period (September to and including December, 1952) fundus changes were seen in three other infants. In two, these changes were very

mild, transient, and required no treatment.

The only other case seen was that in a child who had delayed breathing at birth and had to be kept in a resuscitator for some time afterward. When admitted to the nursery, his condition was very poor and he had marked respiratory retraction.

The initial ocular examination in this case revealed marked retinal edema, multiple retinal hemorrhages, dilated vessels, and such gross vitreous hemorrhages that not even a red reflex could be obtained from the posterior pole. It was assumed that this ocular damage was due to hypoxia which occurred at birth.

The child was treated with oxygen for several weeks, showed complete regression, was weaned from oxygen successfully, and discharged with ophthalmoscopically normal eyes. Subsequent examinations were negative except for the presence of myopia in both eyes.

During the first seven months of 1953, mild vascular dilatation and mild edema of the extreme peripheral retina were observed in four babies who were injudiciously weaned more rapidly than is the usual routine (all showed spontaneous regression to normal in a relatively short time).

Moderate hemorrhages, neovascularization, and moderate vascular engorgement occurred in one child, who, because of his poor condition, required oxygen in high concentration and was subjected to a hypoxic insult when the tubing to his incubator was accidentally disconnected for several hours. This child has normal fundi to this date but is still in a moderately enriched atmosphere (40 percent).

Except for certain fundus changes which were seen in several babies shortly after birth and which will be described later, no other cases of hypoxic fundus changes (early retrolental fibroplasia) were seen.

It is not the purpose of this paper to present more evidence to show that retrolental fibroplasia is induced by interference with oxygenation, nor that it is reversible by oxy-

gen administration; but rather to describe certain fundus changes which have been observed in the study of over 600 premature babies, the relationship of oxygen and other factors to these changes, my experience in the use of oxygen, and the conclusion to which my observations have led me.

TERMINOLOGY AND CLASSIFICATION

If the precursory changes of retrolental fibroplasia can be induced in an infant by removing him suddenly from a highly enriched oxygen atmosphere, if they can be reversed by restoring the available oxygen in high concentration, and if they can be prevented from recurring by gradually weaning the infant into a normal atmosphere, then the typical case of retrolental fibroplasia with blindness, microphthalmos, shallow anterior chamber, atrophic iris with synechias, totally detached and fibrosed retina can justifiably be considered a terminal stage of uncompensated ocular hypoxia. Yet, this gross pathologic termination is admittedly only one of the terminal pictures which follow what, heretofore, has been called early retrolental fibroplasia.

It cannot be denied that any premature baby with retinal edema, dilated and tortuous vessels, neovascularization with or without hemorrhages may, in the end, have either normal-appearing eyes or defects ranging from myopia to marked ocular fibrosis. It is time that some order should be brought into the confusion which now exists in the terminology (and in our thinking) relative to hypoxic ocular damage.

I propose therefore:

1. That the term, "hypoxic retinopathy," be used to designate those retinal changes which heretofore have been called early retrolental fibroplasia and are characterized by retinal edema with or without elevation, and vasodilatation with or without exudation, hemorrhages, and neovascularization.

2. That the term, "ocular fibroplasia," be used as descriptive of the most severe terminal stage of hypoxic retinopathy (though

admittedly it is terminal not only to retinal but also to ocular hypoxia) characterized by enophthalmos, microphthalmos, shallow or nonexistent anterior chamber, atrophic iris with synechias, and a total retrolental fibrotic mass.

3. That the term, "retrolental fibroplasia," be used to designate that terminal stage of hypoxic retinopathy which is characterized by a relatively normal anterior segment but with definite ophthalmoscopic evidence of retrolental pathology consisting of either a total or partial retrolental mass.

4. That "retrolental fibroplasia" as defined above be divided into three grades:

Grade I. Grade I retrolental fibroplasia is characterized by a peripheral mass or masses of white or grayish tissue and the following changes in the rest of the fundus:

Vitreous: Clear or clouded by few or many floating opacities. Rarely a thin transparent membrane may be present immediately behind the lens.

Disc: Normal but often distorted. It may be kidney-shaped with the hollow directed toward the temporal periphery or stretched into a horizontal ovoid. Rarely the disc and surrounding retina may be covered by a sheath of glial tissue so that it is scarcely recognizable.

Retinal vessels: Usually tortuous. May be attenuated. May leave the disc normally but usually are markedly displaced temporally and may appear to emerge from the hollow of the disc (if it is kidney-shaped) or from one small temporal sector if the disc has been distorted into an ovoid.

Retina and choroid: May be pale or pigmented with coarse dark granules. Often there are scattered areas which resemble old healed chorioretinitis or patches of irregular glial tissue proliferation.

Grade II. Grade II retrolental fibroplasia is characterized by a partial retrolental mass with some visibly attached ret-

ina. Retinal folds extending to the posterior pole should be included in this classification. The changes in the rest of the fundus may be identical to those already described.

Grade III. Grade III retrolental fibroplasia is characterized by a total retrolental mass with no visible attached retina.

5. That the term, "retinal fibroplasia," be applied to that terminal stage of hypoxic retinopathy characterized by changes identical to those described under retrolental fibroplasia Grade I but showing no detachments and no peripheral masses or elevations. The visual acuity is usually poor and the eye highly myopic.

6. That myopia be considered as one of the terminal stages of compensated ocular hypoxia not only in premature but also in full-term babies. Any student of this disease cannot fail but be impressed by the extraordinarily high incidence of myopia in children who have at one time shown evidence of hypoxic retinopathy.

It is not only possible, but most likely, that not only the retina but also the developing sclera is damaged during an episode of hypoxia. Mention is made in the literature of intense choroidal congestion and of scleral thinning in microscopic studies of eyes with retrolental fibroplasia.

Ingalls, in describing the sclera of mice which were damaged by hypoxia, states: "The sclera with its attached extrinsic muscles was clearly made out. It showed occasional swelling by edema and frequently irregularly undulating outline."

Embryologically, it is known that the posterior part of the sclera is last to develop. It is not unreasonable to assume that, since the choroid, the retina, and the retinal vessels respond pathologically to hypoxia and since the vitreous is also damaged secondarily through transudation and hemorrhages (and eventually by fibroplastic and angiomatous invasion), the sclera is also damaged, either primarily or secondarily to the structures so intimately in contact with it.

If the sclera undergoes only slight or moderate damage, scleromalacia probably ensues and the posterior segment enlarges simply from the stretching caused by the normal intraocular pressure. If scleral damage is severe, fibrosis probably takes place and the contraction of the fibrous tissue causes the development of a microphthalmic eye.

The frequency of moderate to marked pigmentary changes which follow compensated hypoxic retinopathy and the similarity of these changes to those found in myopia cannot be purely coincidental.

Recently, I have been questioning the parents of all highly myopic children as to their birth weights, circumstances at birth, and age at which the child began to sit, stand, and walk. This study has been most revealing. The incidence of prematurity or a history compatible with hypoxia at or about the time of birth is significantly greater in congenitally high myopes.

Also, the high myope often gives a history of delayed development of his motor functions. He is often late in sitting, late in standing, and very often 15 or more months of age before he begins to walk.

Could it be that the motor centers are in the same state of oxygen want at the time that the eyes are injured by hypoxia and that these motor centers also undergo some hypoxic damage?

METHOD OF EXAMINATION

To obtain maximal dilatation of the pupil, five-percent homatropine and 10-percent neosynephrine were used routinely for several months at our hospital. One drop of each solution was instilled about 30 minutes prior to examination. This was discontinued when one of the babies whose eyes were so dilated developed a stupor which lasted about 10 hours.

At the present time a solution containing 2.5-percent homatropine and five-percent neosynephrine is administered about 30 or more minutes before examination. This has been used on several thousand occasions with no noted ill effects. Dilatation has been

satisfactory in all cases except those in which the iris was engorged during acute hypoxic retinopathy or in which synechias had formed.

Examinations are made on a waist-high table with the nurse holding the baby's head steady. The lids are held apart with the thumb and index finger of one hand. Occasionally, a small lid retractor is placed in the lower cul-de-sac and held by the nurse while the upper lid is retracted by the thumb or forefinger of the examiner. General or local anesthesia is never used. If examinations are made shortly after feeding, and if the examiner is patient, no difficulty should be encountered in making satisfactory observations.

On the initial examination, the condition of the cornea, anterior chamber, iris, and lens may be noted. On subsequent examinations attention is directed entirely to the fundus unless there is specific indication for examining the anterior segments, as, for example, severe hypoxic retinopathy.

With the ophthalmoscope, the clarity of the vitreous is noted and then the attention shifted to the disc and the vessels of the posterior pole. The midperiphery is quickly scanned while the periphery is carefully studied. Particular attention is paid to the size and tortuosity of the vessels, to the abnormal number of vessels, and to the presence or absence of retinal edema.

With practice one may, in a matter of seconds, determine whether there is or is not any sign of retinal hypoxia. Indenting the sclera for examination of the extreme periphery is unnecessary in routine examinations of babies as it reveals no pertinent information.

Not infrequently the fundus view is blurred. The most common causes for this have in my experience been:

1. A collection of mucus on the surface of the cornea. This can often be removed by rubbing the upper lid against the cornea. In some cases a cotton pledget moistened in saline has to be used to remove the corneal film.

2. Remnants of the tunica vasculosa lentis. This is quite common in the very premature babies but it usually does not preclude a satisfactory examination. The tunica regresses after several weeks.

3. Corneal haze which is usually present on the first examination or may appear during an acute conjunctivitis. This haze in most cases probably represents corneal edema following silver-nitrate application. Occasionally, it is so marked that no fundus details can be made out. However, in the majority of cases the haze subsides within a few days.

4. Vitreous opacities may be visualized in some cases. They are usually fine and translucent. From their central location one may deduce that they are remnants of the yet incompletely absorbed hyaloid system.

Occasionally, the vitreous may show a diffuse haze or opacities due to hemorrhage, varying from mild to so gross that only a black reflex is obtained on funduscopic examination. If seen in a newborn child, these opacities are almost always accompanied by dilatation and tortuosity of the retinal vessels, retinal edema, and retinal hemorrhages (evidence of retinal hypoxia at birth).

Since the retinal changes are the first to regress, the immediate cause for this may not be apparent if the child is examined several days after birth. Occurring in an older premature they are again always accompanied by retinal changes due to hypoxia and are part of the picture of hypoxic retinopathy.

During my initial investigation, many babies were examined daily and newborns within the first 24 hours of life, if possible. The present procedure is:

Newborns are examined within the first three days following admission unless their condition is very poor and it is inadvisable to remove them from their incubators even for the short time necessary for examination.

Babies whose fundi are normal on the initial examination and who are not given supplemental oxygen are examined at two week or longer intervals, unless they develop a

respiratory infection or other illness which might make them hypoxic—in which case they are watched carefully.

Babies whose fundi are normal but do require supplemental oxygen are examined at weekly intervals and immediately prior to and within three days after each decrease in the oxygen concentration in their incubators during the weaning period.

Babies who show evidence of retinal hypoxia immediately after birth are examined frequently until the changes subside. Particular attention is paid to them during any illness and during the weaning period if supplemental oxygen administration was necessary for their care.

THE PREMATURE FUNDUS

Because there appears to be some confusion as to what constitutes a normal premature fundus, a brief description is in order.

The optic discs are invariably grayish-white, clearly outlined, and have the appearance of primary optic atrophy. The central cup is filled. The shape is round but not infrequently oval (usually vertically). Occasionally, remnants of the hyaloid system may remain on the surface.

The vessels are usually one-third to one-half the size found in an adult fundus but may at times be threadlike. The vessels are straight, usually branch dichotomously, and decrease in caliber as they approach the periphery. At no time are the vessels enlarged or tortuous nor is there an abnormal number of vessels in the periphery unless as a response to hypoxia. Tortuous, dilated, or an abnormal number of vessels in an otherwise normal-appearing fundus are probably evidence that the retina has been subjected to serious hypoxia in the past but that compensation has taken place.

The color of the fundus is usually orange-red but sometimes yellowish. Frequently, the choroidal pattern is prominent. Pigmentation may be very scant—if present, it is usually very granular. The periphery may be lightly colored and even yellowish-white or

yellowish-gray, but it is not milky or grayish-white unless there has been previous hypoxia.

Hemorrhages, of course, are not a normal finding. They are, however, not infrequently seen if a baby is examined shortly after birth. Streaky hemorrhages near the posterior pole may be due to birth trauma. Blotchy hemorrhages, especially if found in the midperiphery or periphery, are almost always due to hypoxia and, if present, other evidences of retinal hypoxia are evident.

The presence of very dilated and tortuous vessels, moderate to marked peripheral retinal edema, with or without moderate to marked elevation, hemorrhages over and at the base of the edematous retina (a picture identical to the early fundus changes of retrolental fibroplasia) is not at all a rare finding in newborn prematures and even full-term babies.

This picture of retinal hypoxia does not persist for long if it is not severe. Small hemorrhages disappear usually within three days. The dilated vessels return to normal, sometimes within 24 hours. The retinal edema also subsides promptly but often leaves in its stead a pallor of the periphery which differs from edema in that, on close study, fine stippling can usually be made out.

If the changes are severe, regression is slow. Gross hemorrhages, if present, may persist for several days or even weeks. The edematous appearance of the retina anterior to gross hemorrhages will persist until the hemorrhages are absorbed. The vessels may remain dilated for several days or weeks.

These changes have led many observers to the conclusion that dilated vessels and peripheral retinal edema are normal variations in a premature baby. However, it is suggested that they represent a distinct pathologic process.

The regression of these changes is so similar to the regression seen when early cases of hypoxic retinopathy (early retrolental fibroplasia) are treated with oxygen that I

believe they are identical pathologic processes.

In utero, it is generally admitted, the fetus is relatively hypoxic—the oxygen saturation of the blood being probably less than 50 percent. To compensate for this low oxygen saturation the fetus has a relatively high red count.

If prior to or at the time of delivery, a baby is subjected to a sufficiently decreased oxygen intake (decreased oxygen saturation) for a long enough period of time, tissues (like the retina) which utilize oxygen at a very rapid rate will either suffer, or the vascular tree will so adjust itself that more blood is routed to the demanding areas. If this vascular response is not sufficient to meet the demands of a particular tissue, the tissue must either: (1) Die, (2) remain normal but suddenly be able to exist under a most adverse condition (a very unlikely state of affairs), or (3) undergo some pathologic alteration.

My observations lead me to believe that the retina (as an example of a tissue rendered hypoxic) does not die immediately under relative hypoxia, nor does it remain normal in appearance; instead, it responds by becoming edematous. Also, in many cases there is a lag between the onset of hypoxia and the vascular response so that retinal edema often appears before vascular dilatation.

In the eye of a child rendered hypoxic at birth we can, therefore, see retinal edema, vascular dilatation, and often the blood which oozes out of the venous end of the capillaries. Immediately after such a child is born, if he breathes normally, his blood oxygen saturation rises considerably above what it was in utero and prior to the hypoxic episode. He is then in a situation identical to that in a child who has developed early hypoxic retinopathy (early retrolental fibroplasia) and has been placed in an oxygen-enriched atmosphere.

Since the blood now carries more oxygen than the tissues have been acclimatized to, retinal edema regresses rapidly; there being no longer any need for vascular dilatation,

the vessels return to normal size and hemorrhages become absorbed.

Of course, the rate and completeness of the recession will depend on the severity of the damage to the particular tissue and its vascular tree. In some cases the damage may be so severe that it is irreversible.

One may reason from this that, if relative hypoxia at birth causes certain pathologic changes, no matter how severe they may be, which are completely reversed as soon as the child is able to oxygenate himself well, the condition cannot be of great significance. This unfortunately is not quite the case. As will be shown later, a sufficient exposure to hypoxia, even though completely compensated for, may so sensitize some babies that subsequent exposure to hypoxia in early life may cause a response in the same tissues altogether out of proportion to the degree of oxygen lack (want).

HYPOXIC RETINOPATHY

When a premature baby is subjected to a sudden, prolonged, and sufficient decrease in his oxygen intake, as can occur, for example, under certain conditions when a baby is acclimated to a high oxygen atmosphere in an incubator and then suddenly removed, certain changes take place which can be observed and studied in the eye.

The immediate retinal response is edema. This edema appears first in the periphery. All or only one sector of the periphery may be affected. It may involve just the extreme periphery or extend for a considerable distance toward the posterior pole. The affected retina may be relatively flat or elevated. In a severe response, edema may be evident even along the retinal veins in the posterior pole.

Ophthalmoscopically, this edema appears as a milky-white or grayish (occasionally with a greenish tinge) homogenous area in which no details can be made out and similar in appearance to the edema which appears in occlusion of the retinal artery in the adult.

These changes may appear within 24 hours.

If the child compensates rapidly or if sufficient oxygen is administered, these changes regress rapidly. If, however, compensation is slow or insufficient oxygen is administered, the edema may, in part or whole, persist and, within a few days, the originally edematous area becomes pearly white (probably a sign of atrophy).

As the process progresses, this white peripheral area may become elevated and form a fold extending toward the disc, may remain as a white elevated or flat peripheral patch, or may subside and leave in its stead pigmentary changes.

The rest of the retina in these slowly compensated cases does not, as a rule, go undamaged. Depending on the duration and severity of the process, small or extensive areas may turn a yellowish or grayish-yellow color and leave as residua extensive depigmentation or pigment clumping. In many cases complicated by retinal hemorrhages, areas resembling old chorioretinitis or areas of glial tissue proliferation may develop.

Very frequently in these cases, the disc becomes distorted, most likely because of contraction of the peripheral fibrosed areas, and traction on the retina and its blood vessels, so that it becomes kidney-shaped or elongated (usually horizontally), and its blood vessels often become so displaced that they all appear to leave over one small temporal sector. Occasionally in cases in which the posterior pole has been involved by hemorrhages, glial tissue forms and obscures the disc and surrounding retina.

If compensation does not take place, the retina slowly or rapidly becomes detached and eventually a large sector or the whole retina bulges forward behind the lens. The initial separation of the retina is probably due to choroidal exudation.

I have observed gross retinal detachments develop within 24 hours after a hypoxic shock—an interval of time much too short for fibrosis of the retina or the vitreous to

take place and play any important role. Later, however, invasion and organization of the vitreous fixes the atrophic retina in a totally or partially detached position.

The character of the subretinal fluid determines to a large extent the appearance of the detached retina. If, for example, there has been subretinal bleeding, the detached retina will have a reddish-brown hue.

The immediate vascular response is coincident in many respects with the retinal response. Often, however, there appears to be a lag between the appearance of retinal edema and vascular dilatation.

If the retinal edema is limited only to the periphery, the vessels in that region become more prominent. Neovascularization may or may not take place. The large main vessels may or may not dilate.

In a more severe response, there will be a more marked engorgement of the vessels over and at the base of the edematous area, with neovascularization. The main vessels may enlarge and become tortuous.

In a marked response the main vessels enlarge tremendously and at the same time become very tortuous. Transudation and even hemorrhages from the veins take place. The hemorrhages most often appear over and at the base of the edematous retina—though even the posterior pole may be involved. They are always blotchy and may vary from pinpoint to several disc diameters in size.

In a very severe reaction, blood can sometimes be seen distributed along each side of an extremely dilated vein. Occasionally, the first vascular response is not dilatation but the formation of many fine new vessels; then, after one or more days, the main vessels enlarge. This may possibly be due to the occurrence of hypoxia at the very moment that active normal vascularization of the deeper layers of the retina is taking place. The hemorrhages which occur are not due entirely to vascular dilation, for not infrequently they can be seen when only

moderate engorgement and neovascularization have taken place.

If compensation does not take place, the vessels continue to enlarge, grow more tortuous, and new vascular channels become visible. At the height of the process the vessels may be tremendously enlarged and markedly tortuous.

If the vitreous has been damaged by transudation or hemorrhages, newly formed vessels, together with glial tissues, may invade it. When atrophy and fibrosis of the retina begin, the dilatation and tortuosity of the vessels regress until finally they may become attenuated.

If sufficient oxygen is administered to a baby shortly after the vessels become engorged (even though dilatation may be marked), there is a return to almost normal size in a relatively short time (one to three days). Petechial hemorrhages absorb rapidly. Large hemorrhages, however, persist for days or weeks, while the retina anterior to them continues to be edematous and, in spite of oxygen administration, may eventually show residual damage either in atrophy or formation of a fold. If oxygen administration is delayed for several days after the vascular changes have taken place, the dilatation may persist for weeks even though retinal edema subsides and hemorrhages become absorbed.

The vitreous shows a secondary response to hypoxia. Changes in the vitreous are undoubtedly due to transudation and leakage of the cellular elements from the blood vessels as they are not seen unless there is a moderate or marked vascular response. If only the fluid elements pass into the vitreous, they may be recognized by the changes in refractive index which take place, especially at the periphery.

Bleeding into the vitreous may be scant to gross. Gross hemorrhages indicate very severe vascular damage and, if present, usually indicate that the retina has been damaged beyond repair. (However, in two cases

with such gross vitreous hemorrhages that a black reflex was present, oxygen treatment brought complete regression.)

Slight to moderate vitreous hemorrhages may clear almost entirely if the infant's oxygen want is satisfied. In the late stages of the disease, infiltration of the vitreous by fibrous-tissue elements may play an important role in producing total or partial retinal detachment.

In some cases in which the retina and the vitreous have not been irreversibly damaged, invasion of the vitreous by fibrous tissue takes place just posterior to the lens, forming a membrane across the face of the vitreous very similar in appearance to a cyclitic membrane. This can be recognized when the eye is examined with lateral illumination. If the membrane is thin (I have seen three such cases), the fundus can be seen with surprising clarity and may reveal relatively little damage. Babies who have severe retinal elevation and who have little or no vitreous changes may show complete reattachment if their oxygen want is satisfied, and babies with moderate or marked vitreous hemorrhages often have some residual permanent retinal elevation.

The iris, clinically, does not appear to show any changes during the early stages of hypoxic retinopathy except during an acute response. When the fundus changes are severe, the iris may become swollen and its vessels so engorged that they may be visible to the unaided eye. During this stage it responds poorly to mydriatics. Synechias and atrophy follow if the process is not compensated. In cases which have been partially compensated or whose course has been influenced by the administration of oxygen, the iris may show no changes whatsoever.

The anterior chamber usually does not become shallow except during the later stages of the disease. The shallowness may be due to the diminished secretion of aqueous by the ciliary body which is undoubtedly also affected by hypoxia. It would seem probable that it

may also be caused by increased pressure in the vitreous chamber due to transudation and hemorrhages from the blood vessels.

The rapidity of the onset and the severity of the changes described depends on:

1. The degree and duration of the hypoxia.
2. The sensitivity of the baby to hypoxia.

1. THE DEGREE AND DURATION OF HYPOXIA

Hypoxia may be produced in a baby at birth because of difficult labor, premature placental separation or some placental anomaly, hemorrhage, oversedation, and so forth. After birth it may be produced by:

1. Respiratory infections or conditions interfering with respiration.
2. Diseases which produce anemia, or anemia *per se*.
3. Poisons (as carbon monoxide) which reduce the oxygen-carrying capacity of the blood or interfere with oxygenation or oxygen exchange.
4. By sudden reduction in available oxygen, as, for example, transfer from a low to a high altitude.
5. By acclimatization to an enriched atmosphere and too sudden withdrawal. (This, because of the erroneous belief that all or most prematures require supplemental oxygen after birth, is undoubtedly the greatest single cause of retrolental fibroplasia.)

It is important to realize that hypoxia may be an entirely relative condition; that there is a certain absolute minimum of oxygen requirement by a particular tissue but that there also appears to be a relative minimum which is determined by the amount of oxygen to which the tissue has been acclimatized.

In other words if an oxygen-sensitive tissue is continuously supplied with oxygen in excess of its actual needs, it may so adjust its metabolism that it becomes intolerant to a sudden reduction in the amount of oxygen available. Yet, by a very gradual decrease in the available oxygen, the metabolism may

so change that a minimum amount of oxygen is utilized, beyond which reduction is impossible because it cannot support the life of the tissue.

A baby in utero under normal circumstances with the blood carrying a very low saturation of oxygen cannot be considered as being in a state of relative hypoxia because all of his tissues are apparently supplied with sufficient oxygen for growth and development. He could, however, be considered to be in a state of absolute minimum oxygen requirement. A reduction in available oxygen, as can occur at birth, can cause the saturation of oxygen to fall below this absolute minimum and if sufficiently severe or prolonged can produce a pathologic change in those tissues whose needs are not met. In the eye, this pathologic change is evidenced by hypoxic retinopathy.

After birth, as soon as breathing is established, the oxygen saturation of the baby's blood rises considerably above what it was in utero. The degree of saturation depends on several factors: the state of development of the lungs, the depth and regularity of respiration, and the concentration of oxygen in the atmosphere.

After several days, the metabolism of the baby adjusts itself to this new oxygen saturation, becoming intolerant to a sudden or rapid reduction of oxygen but able to compensate to a very gradual reduction. It is for this reason that a severe anemia of sudden onset can cause the appearance of hypoxic retinopathy in one child while an anemia of equal severity but of very gradual onset may be unaccompanied by any retinal response. It is also probably for this reason that hypoxic retinopathy has not been noted to be much more frequent in congenitally blue babies.

In my study of infants whose course was not influenced by severe disease or severe anemia I have noted the following:

1. Hypoxic retinopathy was never found to occur in an infant who had normal fundi at birth and who was not given supplemental oxygen. Over 200 such babies varying in

weight from two to five pounds were studied.

2. No infant who had normal fundi at birth and who was kept in a moderately or even highly enriched oxygen atmosphere for six or less days developed a progressive hypoxic retinopathy. A few did develop a transient retinal response.

3. Of babies who were kept in a low concentration of oxygen (consistently below 40 percent) over seven days, none developed progressive hypoxic retinopathy though a few developed transient changes when they were weaned too rapidly.

4. Of babies who were kept in a highly enriched atmosphere seven or more days, regardless of whether they had normal fundi at birth or not, a vast majority developed either a transient or progressive hypoxic retinal response when they were removed from oxygen suddenly or weaned too rapidly.

5. Of babies who were kept in a highly concentrated atmosphere for seven or more days and who were weaned by very gradual stages to a normal atmosphere without complications, none were observed to develop more than the slightest retinal or vascular response.

6. Of the infants who developed retrolental fibroplasia because of sudden withdrawal or too rapid weaning from an oxygen-enriched atmosphere, the earliest fundoscopic changes were not seen immediately but, in most cases, 24 to 48 hours later. In two sensitized babies the changes developed within three hours.

It appears, therefore, that it takes several days of exposure to an enriched atmosphere for a baby to become acclimatized to it sufficiently so that he could suffer when suddenly removed from it; that the higher the concentration in the baby's initial environment the more severe and more frequent is the appearance of hypoxic retinopathy when supplemental oxygen is terminated too rapidly; and that the hypoxia has to be of sufficient duration to cause a response. Though the severity of the retinal and vascular response is to a great degree proportional to the drop in oxygen concentration to which the baby is

exposed, several other factors influence it considerably.

The role of anemia is extremely important. It is logical to assume that a baby with a high red count would be more likely to compensate for hypoxia than one with a low blood count. My experience has been that anemic babies acclimatized to high concentrations of oxygen seem to develop much more severe reactions when removed from oxygen too rapidly, and that they have to be weaned much more slowly.

Recently, Dr. William Knaus has placed every premature baby on his service into a highly enriched oxygen atmosphere (60 percent or more) and kept them in this high concentration for one or more weeks. Shortly before the babies were to be removed from incubators, a red cell count and hemoglobin determination were made. Anemia, if present, was corrected by repeated transfusions.

When the red cell count was brought up to almost 4,500,000 or more, the babies were suddenly transferred from their highly oxygen-enriched environment to bassinets. Babies whose red count was about 4,000,000 were removed from oxygen without previous transfusions.

The majority of babies who received transfusions and whose count was high immediately prior to withdrawal from oxygen showed little or no recognizable fundus changes following this shock and at no time afterward. A few babies responded by showing retinal edema, vasodilatation, and occasionally small blotchy peripheral hemorrhages; but all of this group to date have compensated of their own accord and have apparently normal fundi.

On the other hand, most of the babies who did not receive transfusions, or whose blood count was not raised sufficiently by transfusions, developed hypoxic retinopathy, and a few had to be placed back into an oxygen-enriched atmosphere because of the progression of the fundus changes.

Although the number of cases studied was too few to draw any certain conclusions, the following suggests itself:

The tissues of an anemic baby kept in an oxygen-enriched atmosphere do not become acclimatized to as high a concentration of oxygen as tissues of a baby with a high red count simply because of the difference in the oxygen-carrying capacity of the blood. Raising, then, the red count of an anemic child by transfusions immediately prior to withdrawal from an oxygen-enriched atmosphere protects him from becoming hypoxic because, though the oxygen saturation becomes less, the quantity of oxygen carried is the same or greater.

Transfusions, therefore, prior to the onset of retinal changes, may be given safely and seem definitely to aid the baby in compensating during his transfer from an oxygen-enriched atmosphere. Transfusions after hypoxic retinopathy has developed—and especially if there is leakage of blood from the retinal vessels—are contraindicated and extremely dangerous. I have noted severe intra-ocular hemorrhages following transfusions in babies with hypoxic fundoscopic changes on several occasions.

It is quite logical that this should occur. If the capillaries are already in such a state that they allow serum or blood to escape through their walls, any increase in the blood volume or pressure would increase the amount escaping. Repair of these walls by increasing the oxygen carrying capacity of the blood would have to be immediate in order to prevent hemorrhages.

In the series of 147 cases (September, 1951, to April, 1952) herein reported, total vision was lost in one eye and that loss can be attributed directly to transfusions during a period of time when the retinal vascular tree was in such a state that it could not withstand an increase in blood volume.

Because of failure to wean him slowly enough, this one baby began to develop hypoxic retinopathy shortly after he was removed from an incubator. He was not placed back into an oxygen-enriched atmosphere until it became evident that he was unable to compensate. Within a short time after the baby's oxygen requirement was met,

beginning regression of the fundus changes was noted.

During this period of regression, the baby was given a transfusion. When examined 24 hours later there were fresh hemorrhages in one eye and such a gross vitreous hemorrhage in the other eye that all details were obscured.

Several days later the baby received another transfusion. On the following examination a severe vitreous hemorrhage was noted in the other eye.

After keeping the baby in an incubator for several weeks, the vitreous gradually began to clear but organization took place and all of the retina of one eye became detached while the other eye fortunately developed only a peripheral retinal fold.

Respiratory infections *per se* produce hypoxia by mechanical interference with respiration. They are especially dangerous when they occur during the weaning process of a child acclimatized to high oxygen concentration.

2. THE SENSITIVITY OF THE BABY TO HYPOXIA

Ingalls, in 1948, reported a high rate of multiple births, toxemia of pregnancy, placental diseases, and hemorrhages among mothers of 41 babies in whom encephalo-ophthalmic dysplasia developed. He hypothesized that sublethal anoxia was the principal agent in the production of this disease.

In my study, I have repeatedly noted that many of the babies in oxygen incubators, who had been subjected to one or more marked prolonged drops in the oxygen concentration in their environment (as for instance, when the incubator vents were opened accidentally over night), showed an abnormal vascular and retinal response each time the oxygen concentration was lowered in their incubators during the weaning-off process.

I have observed several babies who developed hypoxic retinopathy on two or more oc-

casions while in incubators with an oxygen-enriched atmosphere. Each attack was coincident with an unforeseen failure of oxygen supply which was not discovered until the concentration was measured in the incubator. Almost without exception, the second attack of hypoxic retinopathy was more severe than the first, appeared to be more sudden in onset, and frequently was characterized by retinal and vitreous hemorrhages.

A few babies who were discharged with normal-appearing fundi developed hypoxic retinopathy several days to weeks later under circumstances suggesting hypoxia. While in most cases the retinopathy occurred during respiratory infections, one case, also showing anemia, followed a diarrhea of 24 hours' duration, and another occurred during an acute glomerulonephritis with anemia. Two cases were so severe that oxygen therapy was instituted, and one of these progressed to retrolental fibroplasia in spite of therapy. This baby, however, had detachments of one half the retina of both eyes and severe vitreous exudation at the time treatment was started.

The significant point is this: All of these infants had had at one time or another, while under our observation, a previous attack of hypoxic retinopathy which either regressed spontaneously or regressed because of supplementary oxygen administration.

CASE REPORTS

The following cases are particularly interesting:

CASE 1

Baby V. S. weighed 4 lb., 11 oz. at birth. The delivery was noted as being difficult and prolonged. On the first examination shortly after delivery, it was noted that the vitreous was hazy, the vessels dilated, the periphery edematous, and that there were scattered punctate hemorrhages in the temporal periphery of the left eye. Oxygen was administered for less than two days.

The baby was discharged with apparently normal eyes after spending 16 days in the nursery. It was subsequently observed by a local ophthalmologist. Three weeks later the baby was rushed back to the hospital because of acute fundus changes.

Examination revealed a vitreous hemorrhage in the right eye and so gross an hemorrhage in the vitreous of the left eye that only the periphery could be studied. Dilated retinal vessels, peripheral retinal edema, and a large broad hemorrhage in the nasal periphery were also present in the right eye. Medical investigation revealed an acute glomerulonephritis and anemia.

The baby was placed in an incubator and oxygen in high concentration was administered.

After spending seven weeks in the incubator and after gradual weaning, the vitreous of the right eye cleared entirely while that of the left cleared to the point where a good view of the fundus could be obtained. The retinal vessels returned to normal. All hemorrhages and edema disappeared. When re-examined at the age of six months, both eyes were essentially normal except for a few vitreous opacities in the left eye.

CASE 2

Infant L. A. weighed 3 lb., 5.5 oz. at birth. Delivery was uncomplicated. The infant was kept in an oxygen-enriched atmosphere for 20 days.

On the day following removal from its incubator, dilatation and tortuosity of the retinal vessels were noted. For the next three weeks the fundus picture gradually grew worse. At the height of the process the vessels were three to four times their average size and very tortuous.

A moderate number of newly formed vessels were seen in the midperiphery and extreme periphery; blotchy hemorrhages in the superior periphery of both eyes and the temporal midperiphery of the right eye; well-defined elevated white areas in the superior and superior temporal periphery of the right eye; a flat gray-white area in the superior periphery of the left eye. During the next four weeks the vascular changes regressed and hemorrhages disappeared.

At the age of three months, except for the persistence of the peripheral white areas in the right eye, the fundi were essentially normal. The baby was examined at regular intervals thereafter.

At the age of six months the child developed an upper respiratory infection. Coincident with this, many fine vitreous opacities and a large blotchy retinal hemorrhage developed in the right eye; the left eye remained normal. No treatment, except for the respiratory infection, was given. After approximately six weeks, the hemorrhage absorbed and the vitreous cleared.

When examined at the age of nine months, the only unusual ocular findings noted were granular pigment deposits and a marked myopia of the right eye.

On one occasion two babies who had been previously severely damaged by hypoxia were subjected to a change from 50-percent oxygen atmosphere to one of 21 percent.

Both infants had previously been treated with oxygen because of hypoxic retinopathy and both had relatively normal fundi prior to the change in oxygen concentration. Within three hours both developed marked vascular engorgement, marked retinal edema with elevation of three to four diopters, and many fresh hemorrhages.

I believe, therefore, that children who are subjected to previous hypoxic episodes because of: (1) Disease during pregnancy which interferes with oxygenation, (2) placental anomalies, bleeding, (3) drugging prior to or at time of delivery (twilight), (4) deep anesthesia at the time of delivery, (5) multiple pregnancies, (6) uncontrolled oxygen concentration in the incubators—so that the baby is exposed to periods of high- and of low-oxygen concentration—become hyper-reactors to any sudden, even slight, decrease in their oxygen intake.

These are the babies who are most likely to develop the progressive changes which end with ocular or retrolental fibroplasia. Not only is the retinal and vascular response more severe, but the time interval between onset of hypoxia and the development of visible changes considerably shortened.

This may readily be the explanation:

When the oxygen saturation of the blood falls to the point that it just meets the requirements of the retina, or is below its requirements, the retina will utilize all the available oxygen leaving the venous ends of the capillaries so oxygen poor that the venous walls suffer from hypoxia or even anoxia.

During this period of time they become lax, dilate, and undergo a certain amount of damage. When the proper oxygen saturation is restored shortly afterward, the dilatation disappears but the walls are left in a hyper-sensitive state so that when the hypoxic insult is repeated they dilate more rapidly; leakage of serum and blood occurs much more readily. Repeated insults make each succeeding response to hypoxia more severe and more abrupt in onset. In some babies, after they have been kept in an incubator

with a constant oxygen level for several weeks, this abnormal reactivity seems to disappear.

From these observations it therefore appears that, although the severity of the retinal and vascular response is to a great degree proportional to the drop in oxygen available to the baby, yet it is the sensitivity of the baby to hypoxia, as well as the degree of anemia present, which to a great extent determines whether the response will be mild or marked, transient or progressive.

STAGES OF HYPOXIC RETINOPATHY

Because of the great variability in the onset and the rate of progression of hypoxic retinopathy, no classification will perfectly define every picture which may present itself. However, by grading the severity of the changes and dividing the progression into stages a useful clinical classification can be made.

STAGE I

The reversible stage. The immediate retinal and vascular response

This is the stage which includes those changes which appear in a matter of hours after a baby is subjected to hypoxia. Contrary to usual reports in the literature, retinal edema appears very early and often precedes visible vascular dilatation or neovascularization. It can roughly be divided into the following grades:

Grade I is characterized by peripheral retinal edema (white, or grayish-white, homogenous appearance) involving all or only a sector of the periphery. There is little or no vasodilatation and little or no visible neovascularization. The vessels over the edematous area may appear prominent. There are no hemorrhages and no visible vitreous exudation. The midperiphery and posterior pole are entirely normal. The anterior segments show no changes.

Grade II is characterized by more extensive peripheral edema which may involve all of the periphery or be limited to a sector.

There is moderate to marked vasodilatation with or without moderate neovascularization in and about the areas of retinal edema. Hemorrhages may or may not be present. They are always blotchy in nature and situated usually at the base of the edematous retina. The anterior segments are normal.

Included in this Grade II are the occasional cases which show as the initial change a diffuse neovascularization involving first the midperiphery and periphery with no dilatation of the main vascular channels. The retina in the involved areas usually has a grayish-yellow or grayish-orange appearance. The neovascularization rapidly spreads to the posterior pole.

Grade III is characterized by a marked peripheral retinal edema, usually with elevation. There is marked vascular dilatation and tortuosity. Neovascularization and hemorrhages are common. There may be transudation into the vitreous. The anterior segments are normal.

All three grades of Stage I are completely reversible either by compensation on the infant's part or administration of oxygen.

Infants showing Grade-I changes 24 to 48 hours after they are removed from an oxygen-enriched atmosphere (or when the oxygen concentration is significantly lowered in the incubator or as a response to an upper respiratory infection) will, in the majority of cases, compensate and the condition will regress spontaneously.

Occasionally, a baby with these changes will progress to Stage II or, since the baby's oxygen demand and oxygen supply are in a precarious balance, a slight interference with oxygen intake or oxygen-carrying ability (as progressive anemia) may cause him to develop Grade-II and even Grade-III changes.

Most of the babies in Stage I with Grade II changes will also show spontaneous regression, but again such a baby can easily develop Grade-III changes or progress into Stage II.

Many, if not most, of the babies with Grade-III changes will show progression. If

the baby compensates, the changes regress very slowly and there may be some residual ocular damage, either in pigmentary changes, retinal fibroplasia, myopia, or possibly a retrolental fibroplasia Grade I. If oxygen is administered in sufficient concentration, regression is prompt and dramatic.

If, on examination 24 to 48 hours after removal from an oxygen-enriched atmosphere or after the concentration of oxygen in the incubator has been significantly lowered, the baby shows Grade-III changes, he should be immediately placed back into an oxygen-enriched atmosphere or the concentration significantly raised; if Grade-I or Grade-II changes are present, examination should again be made in two to three days; if there are signs of progression, oxygen should be administered or the concentration raised.

STAGE II

The active stage. Beginning of irreversible changes

This stage follows in one or several days after the onset of the changes of hypoxic retinopathy. It is characterized by beginning retinal atrophy, an increased vascular reaction, and frequently by changes in the vitreous.

Grade I. The originally edematous peripheral retina becomes pearly white or grayish-white in color. Frequently, the changes become limited to one sector of the periphery—usually temporally. Elevation, if present, is not marked. The vascular engorgement and tortuosity may be generalized or it may be limited to the vessels leading to the involved retina. Occasionally, small blotchy hemorrhages are seen. The vitreous is not cloudy, but there may be some exudation in the periphery. The anterior segments appear normal.

Grade II. The edematous retina becomes definitely elevated. Its color may be pearly white, gray, greenish gray, or, occasionally, reddish brown. All or a large sector of the periphery may be involved.

The vessels become very engorged and

tortuous. Neovascularization may be moderate to marked and greatest over and at the base of the involved retina. Blotchy peripheral hemorrhages are frequent. Exudation with hemorrhage into the vitreous is not uncommon but usually not marked.

The retina of the posterior pole may show small or extensive areas which turn to a yellowish or yellowish-gray color and may also show moderate or marked neovascularization.

In cases which start initially with neovascularization, the peripheral retina becomes definitely edematous and may even be elevated. The entire fundus may become covered with fine newly formed vessels. The iris may become edematous and the anterior chamber somewhat shallow.

Grade III. Usually, all or most of the peripheral and midperipheral retina becomes elevated and its color is similar to that seen in Grade II. The posterior retina may show extensive edema.

The vessels become markedly dilated and tortuous. Neovascularization may be moderate or very marked. There is usually marked vitreous exudation and hemorrhages so that frequently the fundus view is blurred. The iris may show moderate or marked edema. Dilated vessels may be visible on its surface.

Babies who compensate during this stage usually have some residual ocular damage. This may range from myopia to retrolental fibroplasia Grade II. If oxygen is administered, the residual ocular damage will be considerably decreased.

Regression when oxygen is administered during this stage will not, as a rule, be dramatic. The longer the changes are allowed to progress, the slower and less dramatic will be the response to treatment. In many cases, days will elapse before any significant improvement is noted and often a child in this stage has to be kept for several weeks in a highly oxygen-enriched atmosphere (we have kept babies in this stage in oxygen for as long as 12 to 16 weeks).

STAGE III

The irreversible stage

This stage is characterized by permanent vitreous changes and retinal atrophy. Oxygen administration will not reverse the process. It may, however, prevent Grade-I changes from developing into Grade-II or Grade-III changes if there is some additional interference in oxygenation of the baby during this stage.

Grade I. The involved peripheral retina, usually the temporal sector, is pearly white, elevated, and may be raised in a tent fashion. It is clearly outlined and rather sharply delimited from the posterior retina which may be relatively normal in appearance.

The vessels are moderately or even markedly engorged and tortuous. The vascular dilatation may be limited to those leading to the involved sector. Neovascularization is not marked. Fine vitreous strands may be visible over the atrophic retina. The disc is often distorted, elongated vertically, or kidney shaped. The retinal vessels are usually displaced temporally. The anterior segments may be normal.

Grade II. All of the periphery may show elevation of the retina of several diopters, or a sector of the retina may show extensive detachment extending to the posterior pole. The color of the retina may be white, various shades of gray, or reddish to reddish brown.

The vessels are very engorged and tortuous. Neovascularization may be moderate or very marked. Hemorrhages are frequent.

Organizing strands can be seen in the vitreous and may even pull the retina into a tent-shaped elevation. The disc, if visible, is usually distorted.

Grade III. There is extensive detachment of the retina involving all or almost all of the retina with elevation of several diopters. The color is similar to that of Grade II. The vessels are markedly engorged and tortuous, and there is usually extensive neovascularization.

The vitreous shows many opacities and organizing bands. Occasionally, there is such

gross bleeding that only a black reflex can be obtained. The anterior chamber is definitely shallow. The iris is usually atrophic and often adherent to the lens.

STAGE IV

The terminal stage

The retinal vessels return to normal or become attenuated. The damaged vitreous becomes organized.

Grade I terminates with (1) retrolental fibroplasia, Grade I, or retinal fibroplasia.

Grade II terminates with retrolental fibroplasia, Grade II or Grade III.

Grade III terminates with (1) retrolental fibroplasia, Grade III, or (2) ocular fibroplasia.

OXYGEN ADMINISTRATION

Knowing that a baby is in a state of minimum oxygen requirement in utero and has a relatively great oxygen-carrying capacity at birth (because of high red count), it makes little sense to saturate him with oxygen immediately after birth. The routine use of oxygen in high concentrations for all premature babies is as logical as insisting that each premature take four ounces of formula at each feeding regardless of whether he is two or five pounds of weight.

It is much more logical to give supplemental oxygen when it is needed and in concentrations just sufficient to meet the deficiency which is present. The indiscriminate use of oxygen in the care of premature babies is to be condemned, not because oxygen itself is toxic and responsible for the development of fibroplasia but because of the great danger of acclimatizing a child to an abnormal atmosphere, sensitizing him, and causing a relative hypoxia when oxygen administration is terminated.

The theory that retrolental fibroplasia is caused by the toxic effect of oxygen is not tenable for various reasons:

It cannot account for the presence of funduscopic changes, identical to those which eventually lead to fibroplasia, in some babies immediately after birth.

It cannot account for the development of these changes days or weeks after birth or after oxygen has been discontinued under circumstances compatible with hypoxia.

It cannot account for the dramatic improvement noted when babies with fundusoscopic changes of short duration were treated with high concentrations of oxygen (an observation reported by me and confirmed by Jefferson). Nor can it account for the fact that these babies could be kept in very high concentrations of oxygen for several weeks and the development of any ocular changes could be prevented by very gradual weaning.

Prior to our interest in retrolental fibroplasia almost all babies on admission to our nursery were administered oxygen. When it was decided to reduce the use of oxygen to a minimum, it was found that over half the babies admitted did not need any supplemental oxygen and that, of the group that did, many required it only for a short time.

Contrary to common belief, all prematures regardless of birth weight do not require supplemental oxygen. The majority of babies will thrive and develop well in a normal atmosphere. Of the few who do require supplemental oxygen, the number could probably be reduced significantly by avoiding a hypoxic insult prior to or at the time of delivery (twilight and anesthesia.)

One of the most important decisions to be made when a newborn premature baby is brought to the nursery is whether he does or does not require supplemental oxygen. The color of the baby and its breathing is probably the best index. If the baby is pink, one can be sure that the baby is well oxygenated.

This criterion cannot, however, be applied to babies who have become acclimatized to high oxygen and then removed. As was pointed out previously, these infants show no changes in color or breathing—the hypoxia which develops is relative. Such transient attacks of cyanosis as can occur, for example after feeding, are no indication for continuous oxygen administration.

Once it has been decided that a baby does

not need supplemental oxygen, and if the fundi are normal or show no significant hypoxic change, one can almost be sure that such a child will at no time later develop progressive hypoxic retinopathy unless he should develop a sudden illness which would cause a prolonged hypoxia.

When a baby's condition is such that continuous oxygen administration is indicated, he should be placed in a minimally enriched atmosphere which is just sufficient to prevent cyanosis and/or labored breathing.

This minimum concentration should be determined by the use of a reliable oximeter and not solely by manipulation of the oxygen-flow valve. Once this minimum has been determined every effort should be made to keep this concentration of oxygen constant. The concentration should be measured with an oximeter at regular intervals.

All nurses and personnel engaged in the care of babies in incubators should be properly instructed in oxygen administration and repeatedly reminded to be always on the alert to prevent accidents which would influence the proper flow of oxygen to the incubators (for example, pinched or disconnected tubing, accidentally opened vents, faulty valves, worn-out gaskets on the water filter jars, cracked or improperly fitting filter jars, and so forth).

If a baby improves rapidly and appears not to require prolonged oxygen administration, an attempt should be made to wean him to a normal atmosphere within the first week. This can be done rapidly in most babies provided they do not have fundusoscopic changes or significant anemia.

Once a baby has, however, become acclimatized to an enriched atmosphere (this apparently takes about one week)—and since it is usually impossible to differentiate the sensitized from an unsensitized infant—weaning should be done in very gradual stages. The goal to be aimed for is the prevention of any fundusoscopic changes. The weaning period should be begun when it becomes apparent that the baby can survive

without supplemental oxygen, but only if the fundi show no evidence of hypoxia.

The presence of hypoxic retinopathy in a well baby, who had previously normal fundi, while in oxygen, is an indication that the incubator's oxygen supply has either been discontinued or significantly lowered on one or more occasions. Before weaning is begun, such a baby, if the fundus changes are not severe, should be kept in the same concentration until all the changes regress. If the fundus changes are severe, the concentration of oxygen should be raised significantly above the original level and kept high till maximum regression has taken place.

If anemia is suspected, a red cell count and hemoglobin determination should be made. Transfusions, if indicated, should be given while the baby is still in the initial concentration of oxygen and only if the fundus findings are negative or show no significant hypoxic response.

Weaning a child to a normal atmosphere is not a simple procedure. It requires constant care, alertness, and frequent use of the oximeter. After much trial and error, the following procedure has been found most satisfactory for normal prematures.

The oxygen concentration is lowered in increments of 20 percent of the highest concentration at seven- to 10-day intervals. For example, if the initial concentration was 60 to 65 percent, a reduction to about 48 to 52 percent is maintained for about one week. The next reduction would be to 38 to 42 percent, then to 30 to 35 percent, 25 to 30 percent, and, finally, to atmospheric concentration, with each stage maintained for about one week to permit acclimatization.

A funduscopy examination immediately prior and shortly after each lowering of the oxygen concentration is very important as it determines whether the weaning process should be more prolonged.

After a baby has been successfully weaned into a normal environment, funduscopy examinations at one or several week intervals are usually sufficient. After discharge, his

sensitivity to oxygen changes should not be forgotten. The parents must be warned to protect the baby from possible respiratory infections and to provide adequate ventilation at home, especially if the child is discharged during cold weather when the home may be heated by a coal or oil stove often kept in the same room as the baby.

It is also well to advise the parents to return the child for an ocular examination during any severe illness, and especially if the child had at one time greater than Grade-I hypoxic changes at birth or during his stay in the nursery.

Using the procedure outlined above, my experience has been most gratifying and the number of ophthalmoscopic examinations necessary has been considerably reduced. Since this method of care for premature babies has been adopted, the death rate, instead of rising, has fallen and the only babies who have presented any problem as far as prevention of retrolental fibroplasia is concerned are those whose initial condition was so poor that oxygen in high concentrations was necessary to sustain life and who developed either a severe upper respiratory infection or severe anemia while in the high concentration of oxygen.

With the rational use of oxygen and proper attention to respiratory infections and anemia, the number of babies developing any degree of hypoxic retinopathy should be insignificant.

The criteria used to determine whether hypoxic retinopathy is to be treated are: (1) Progression and (2) the severity of the response.

As was previously stated, hypoxic retinopathy may be present at birth. If the changes are not severe, regression usually takes place without supplemental oxygen administration. If, however, the funduscopy change is severe and especially if there are vitreous hemorrhages, it is probably best to treat such a child in the same manner as one who develops this condition because of too rapid withdrawal from oxygen, because of

interference with his oxygen supply while in the incubator, or because of an illness which produces hypoxia.

Originally, early cases of hypoxic retinopathy were treated by administering oxygen in high concentrations (60 percent). Then, for a short time, an attempt was made to treat them with lower concentrations or by restoring the concentration to what it was prior to the hypoxic insult.

My success with the higher concentrations was so much more satisfactory that now routinely any child who requires treatment is placed in an oxygen atmosphere that is significantly higher than it was prior to the onset of the hypoxia. The concentration is then kept constant until all fundus changes have regressed or until maximum improvement has taken place before gradual weaning to a normal atmosphere is begun. The manner of weaning is similar to that already described.

It is extremely important that treatment be started early. The longer the changes are allowed to progress the slower will be the response to treatment, and the more likely will be residual ocular damage. Early cases will respond dramatically in 24 to 48 hours. More advanced cases may be so slow to respond that days may pass before any visible improvement is noted. Because it is difficult to determine when the latter have regressed maximally, the status of the retinal vessels is used as an index. When the vessels have returned to normal size, one may assume that no further improvement will take place and weaning can be begun.

It is also of the greatest importance that, while a child is in an oxygen-enriched atmosphere because of hypoxic retinopathy, he not be again subjected to a sudden prolonged drop in the supplemental oxygen.

It appears that most, if not all, children who have developed progressive hypoxic retinopathy are extreme hyper-reactors when subjected again to the same insult. The second or third response to prolonged hypoxia is often very violent and usually associated

with marked hemorrhages in the retina and the vitreous.

After successful treatment and uneventful weaning, a child must be kept under observation for several months after discharge. Any subsequent illness which could cause anemia or respiratory difficulty should be viewed with alarm.

Transfusions during hypoxic retinopathy are of course contraindicated. It is best to postpone the administration of blood till a definite improvement has taken place in the retinal vascular tree.

INCUBATORS

A word about incubators seems appropriate at this time. To be efficient and safe the ideal incubator should have the following features:

1. No seams which could leak; no lids or adjustable vents.
2. Port holes with efficient covers so that the infant can be fed and attended without removal from the incubator.
3. An oxygen inlet tube placed away from the head of the infant and equipped with one adjustable valve which would automatically mix oxygen with air in the desired concentration before it diffuses into the incubator. The valve should be attached to the incubator at such a position that it is always visible to the personnel in the nursery and it should have an indicator which will show when the oxygen is flowing properly.
4. An opening for the escape of air of such size that positive pressure does not build up in the incubator and in such a position that temperature or air currents have negligible effect on the oxygen concentration.
5. Automatic control of heat and humidity.

Because of the great difficulty we experienced in controlling the oxygen concentration in our hinged-lid incubators we have equipped most of our incubators with a simple venturi-type valve with its output nipple inserted through a hole at the foot end of the incubator. In this valve air mixes with oxygen before it enters the

incubator. The amount of air entering is controlled by a disc with varying sized holes.

When the maximum amount of air is allowed to enter the valve, the concentration of oxygen at the output nipple is about 36 to 40 percent. When the oxygen is flowing at four liters per minute, approximately 13 to 16 liters of air are sucked into the valve so that 17 to 20 liters of diluted oxygen enter the incubator per minute. This great flow minimizes the effect of ventilation in the incubator and, while not entirely satisfactory, at least allows a greater control over the oxygen concentration and prevents the development of high levels.

Lower levels of oxygen concentration are produced by manipulation of the vents or the cover of the incubator. Often a diaper is placed under the lid so that it is partially open and not infrequently a baby spends its final week in the incubator with the lid wide open while the oxygen is still flowing.

THEORY

If it is true that various tissues and organs utilize oxygen at a widely varying rate and that neural tissues, especially highly specialized neural tissues, have high oxygen requirements, then it must follow that, if the oxygen content of the blood is suddenly decreased, although it may meet the requirements of most of the tissues of the body, it may be inadequate for certain oxygen-hungry areas. If the fall in oxygen content is slight, it may just fail to support the most demanding tissues; if more severe, other tissues with high oxygen utilization may be affected unless certain sufficient compensatory changes take place.

When a tissue is subjected to hypoxia, it would seem logical to forecast the following chain of events:

1. Edema of the involved tissue and vasodilatation, in an effort to route more oxygen to the anoxic tissue. If the vascular response were sufficient, regression would follow; if insufficient, the next stages in the pathologic response would follow.

2. Increase in tissue edema. Increase in the vascular bed, vasostasis, capillary damage, escape of fluid and blood.

3. Atrophy of involved tissue.

4. Repair.

Since the changes in the retina of a child subjected to a decreased oxygen intake seem to follow this pattern and since the retina is not an isolated tissue but one similar in origin, similar in metabolism, and similar in its oxygen requirements to other specialized neural tissues, it is not illogical to assume, at least temporarily, that this pathologic response can occur not only in the retina but also in other oxygen-sensitive tissues.

Assuming that during fetal development different areas develop and require oxygen at different rates and that, as development progresses, first one then other areas ascend in their needs for oxygen, and that as a baby nears its full development only certain highly specialized tissues have high oxygen requirements, then the particular tissue involved in a response to hypoxia would depend on the stage of development during which the hypoxia became manifest. An uncompensated hypoxia early in fetal development could be expected to produce terminally gross malformations while a similar insult late in development could be expected to cause more selective damage.

This concept of variability in oxygen requirement during fetal development and selectivity of response to hypoxia can readily account for many observed facts.

1. It can account for Ingalls' experimental production of various types of deformities in newborn mice by subjecting the pregnant mouse to hypoxia of several hours' duration during various days of gestation.

2. It can account for Ingalls' observation that mongolism in the human is apparently due to conditions producing a lack of oxygen at about the eighth week of gestation.

3. It can account for the observation of Reese and Blodi that retinal dysplasia (an ocular condition pathologically identical to ocular fibroplasia except that the involved

retina is more fetal in character) is associated with cerebral agenesis and congenital anomalies elsewhere over the body.

4. It can account for the fact that some observers claim that retrolental fibroplasia is an isolated clinical entity, while others that cerebral involvement is also a part of the disease (encephalo-ophthalmic dysplasia).

If the hypoxic insult should occur at the time when the developing retina is the tissue foremost in oxygen requirement, it is quite possible that only the retina may become involved and irreparably damaged. If the insult occurs at a period of time when other tissues are in the same state of oxygen demand as the retina, or if the hypoxia is severe enough to affect tissues lower in the scale of oxygen utilization than the retina, then a picture of encephalo-ophthalmic dysplasia might logically occur.

My own experience has been that prematures who develop any degree of fibroplasia or high myopia show a definite retardation in development of their motor functions. They are usually late in sitting, standing, or walking. Not infrequently 24 or more months elapse before the child develops sufficient stability to walk. Though some of these children appear to be mentally retarded, it is difficult to evaluate them.

One observation has particularly impressed me. During the past year, three full-term infants (each over seven pounds' weight at birth) with retrolental fibroplasia were seen. In each there was a definite history compatible with severe hypoxia at birth, and all three had severe cerebral palsy and marked mental retardation.

This suggests that, as the child reaches the gestational age of nine months, the oxygen requirements, in certain centers in the brain may rise and may approach or exceed the retina in oxygen utilization. If the retina has passed its critical point of development at full term, and if certain cerebral centers are then in a critical stage of development and high in oxygen requirement, a hypoxic insult at or about the time of delivery could

conceivably produce serious damage in certain neural centers without producing fibroplasia; or, if the hypoxia were sufficiently severe, both could be produced, with the neural damage more extensive. The production of cerebral palsy or similar conditions with or without ocular fibroplasia could then readily be explained.

The observation that the retina can become sensitized to hypoxia by previous exposure and react altogether out of proportion to the stimulus if again subjected to hypoxia may logically also be applied to other tissues. If it is true, then a child rendered sufficiently hypoxic prenatally or at birth can indeed be in a precarious position. If not injured irreversibly by his first experience, he may be left in such a sensitized state that permanent damage might be incurred during a second experience with hypoxia early in life.

CONCLUSION

This, then, seems to be the chain of events which lead to fibroplasia:

In utero or during delivery a child may or may not undergo a hypoxic insult. A hypoxic insult in the majority of babies produces a response in tissues highly sensitive to oxygen changes which completely reverses itself in most babies after birth simply because the oxygen saturation of the blood rises considerably above that prior to the insult. In some cases the insult may be so great that the changes are irreversible. The child, who has been sufficiently injured by hypoxia and has recovered, is, however, left in a state that will make him react abnormally when subjected again to the same insult.

After birth, a child may or may not be given supplemental oxygen in an incubator. Those children who are not given supplemental oxygen are not likely to suffer unless they should suddenly develop some condition which would interfere with their oxygen absorption or oxygen-carrying capacity. Then, the child who had never undergone a previous hypoxic episode would be likely to compensate, while the child sensitized to hypoxia

by previous exposure would show an abnormal reaction in his oxygen-sensitive tissues (retina) and might even progress to the development of fibroplasia.

Infants given supplemental oxygen for a short period of time or during periods of cyanosis are also not likely to suffer because they have not become acclimatized to an enriched atmosphere and do not develop relative hypoxia even when oxygen administration is terminated suddenly.

Infants, however, who are kept in an oxygen-enriched atmosphere for a period of time sufficient to acclimatize them to it would, when transferred too suddenly into a normal atmosphere, respond as follows:

1. The unsensitized infant would probably develop a transient response unless the supplemental oxygen was terminated during a period of sufficiently severe anemia; then severe, probably progressive, hypoxic retinopathy would develop.

2. The sensitized infant would most likely develop a progressive type of hypoxic retinopathy, especially if he had become acclimated to a very high oxygen concentration.

Any infant who is given supplemental oxygen for a long period of time after birth, however, is exposed to the danger of becoming sensitized to hypoxia because of significant variations in the oxygen concentration which can take place in his incubator.

Being aware of the relationship of oxygen to fibroplasia, certain predictions as to the incidence of this disease can be made:

1. Centers where little or no oxygen is used in the care of premature babies and where good obstetrical and pediatric care are provided would have the lowest incidence.

2. Centers where oxygen is used for short periods of time only would also tend to have a low incidence.

3. Centers where oxygen is used routinely even for long periods of time but where, purposely or because of the incubator and the conditions in the nursery, the concentration tends to be low and stable would also have a low incidence.

4. Centers where oxygen is used freely and

indiscriminately and, because of conditions in the nursery, tends to be high and to vary in the incubators will have the highest incidence.

5. Centers where oxygen is used in high concentrations but, because of the incubators and the conditions in the nursery, the concentration tends to be constant during the entire stay of the infants in incubators, will tend to have a lower incidence than those in 4.

6. The incidence will vary little in institutions where little or no oxygen is used. It is possible, however, that cases could occur during severe respiratory infections.

7. The incidence may vary considerably in institutions using oxygen freely even though there is no apparent change in technique for the following reasons:

- a. Worn out equipment—valves, rubber gaskets, and so forth—which would allow significant variations in the oxygen supplied to infants in incubators.

- b. Installation of new or more efficient or less efficient incubators.

- c. Changing the locality of the nursery. If, for example, incubators are transferred from a location where the temperature and air currents tend to stay constant to one where there is a great variation, a rise in incidence could be expected.

- d. Changes in personnel. One individual unfamiliar with oxygen equipment or the proper administration of oxygen can be responsible for the appearance of hypoxic retinopathy in many infants. A nurse may very innocently cause a dangerous change in the concentration of oxygen in incubators by opening windows during her period of duty and thus, by lowering the temperature of the whole nursery, cause a lowering of the oxygen concentration in the incubators.

Any program for the prevention of fibroplasia and other diseases due to hypoxia must of necessity begin with the obstetrician. It must be his duty to see that an infant is not damaged or sensitized by hypoxia prenatally or at the time of delivery.

Some of the precautions necessary are

quite simple—for example, traveling in high altitudes (in plane or car) and over exertion should be forbidden pregnant women; depressing drugs or anesthetics should not be used (or if necessary used with extreme caution) in the delivery of premature babies, multiple babies, or when there is a history which suggests that the infant in utero may have been previously subjected to hypoxia (placental bleeding, severe illness during pregnancy and so forth).

The pediatrician has the responsibility of determining which infant requires supplemental oxygen, in what concentrations, and for what length of time. It is his duty to see that an infant acclimatized to an oxygen-enriched atmosphere is weaned properly to a normal atmosphere and to give proper and prompt care to diseases which interfere with oxygenation or oxygen-carrying capacity.

It is the responsibility of the ophthalmologist to determine which apparently normal babies should have supplemental oxygen

after birth because of funduscular changes, to guide the pediatrician in the care of babies receiving oxygen during the weaning process, and to advise him as to the state of the retinal vessels when transfusions are contemplated.

SUMMARY

Retrolental fibroplasia is considered as one of the terminal phases of uncompensated retinal hypoxia. The stages of hypoxic retinopathy are described, the terminal phases classified. Various factors involved in its causation are considered. A program for its prevention by proper attention to hypoxia and use of oxygen is presented.

215 Metropolitan Building.

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OPHTHALMIC MINIATURE

... If we are indispensably prompted to rub the eyes on first waking, it ought not to be done rudely, but merely by passing a wetted finger over the eye-lids, if we find it difficult to open them.

H. Colburn, London, 1816,
The Art of Preserving the Sight Unimpaired to an Extreme Old Age.

ANGIOMATOSIS RETINAE (VON HIPPEL'S DISEASE) 11 YEARS AFTER IRRADIATION*

FREDERICK C. CORDES, M.D., AND ARIAH SCHWARTZ, M.D.[†]
San Francisco, California

In 1882 E. Fuchs¹ first described the rare disease now known as angiomas of the retina as a traumatic arteriovenous aneurysm. Various other observers reported it subsequently under a number of different titles until von Hippel² established it, in 1904, as an angiomas of the retina.

In 1905 Czermak³ described a case in association with a cyst of the cerebellum, internal hydrocephalus, and cystadenoma of both ovaries, and in 1912 Seidel⁴ reported a similar case in which choked discs were observed, and later, at operation, a cerebellar cyst.

It was not until 1927, however, that Lindau⁵ demonstrated a close association between angiomas of the retina and angiomas and cystic lesions of the central nervous system, particularly the cerebellum, and of such visceral organs as the kidneys, pancreas, ovaries, and suprarenal glands. Since then the condition has usually been referred to as the von Hippel-Lindau syndrome.

CLINICAL PICTURE

Angiomas of the retina occurs most commonly in young adults at an average age of 25 years.⁶ It is bilateral in about 50 percent of cases and the tumors are multiple in some 33 percent. Hemorrhages into the retina and vitreous may occur and are sometimes severe. There is cerebellar involvement in about 25 percent of cases and its signs usually appear some 10 years after the discovery of the ocular lesions.

A review of the literature indicates a definite familial incidence. The disease is usually

transmitted through the female, but 60 percent of cases occur in males.⁷

The fundus picture is characteristic. The retinal change first observed is a marked dilatation of one or more retinal veins. Usually a communication between a retinal artery and the affected vein can be made out; this marks the beginning of the tumor formation.

From this *rete mirabile* a berrylike, reddish-colored mass develops that is sharply demarcated from the surrounding area and is supplied by an artery and a vein, both of which develop into wormlike, enlarged stems carrying dark blood. The retina surrounding the tumor is slightly elevated.

Around the macula and disc, shiny white spots of exudate appear; they are at first pinhead in size but later become confluent.

A globular detachment of the retina always supervenes and surrounds the enlarged tumor mass. It usually develops from the periphery and gives the impression of being semisolid. In this stage the exudate increases in amount and becomes yellowish in color. The condition progresses until there is massive detachment of the retina, marked enlargement of the vessels leading to the tumor, atrophy of the disc, and amaurosis. When the retina is completely detached it often looks as if it lay over, or as if it were permeated by coagulated milk.

Iridocyclitis finally develops and is complicated by secondary glaucoma, and eventually by opacification of the lens.

PATHOLOGY

Microscopically, the angioblastoma is composed of thin-walled capillaries. This would seem to provide a rationale for the use of X-ray irradiation in treating it in view of the effect that X ray is known to have on new-formed vessels. The cells between the

* From the Department of Ophthalmology of the University of California Medical Center at San Francisco. Presented at the 88th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, June, 1952.

[†] By invitation.

vessels show very few mitoses. The feeding vessels are greatly dilated and thickened, and there is a tendency for the tumor to show some cystic degeneration.

Wolff⁸ states that curious fat-laden cells lie between the vessels. In the usual preparation the fat has been dissolved so that the cytoplasm has a honeycombed appearance. A fibro-osteogenic membrane tends to form around the growth.

It is interesting that miliary aneurysms occurring in young individuals, especially males, are associated with marked and progressive changes of an exudative and degenerative nature not unlike the changes in angiomas. Duke-Elder⁹ feels that the diffuse cases actually represent a type of angiomas and are related to von Hippel's disease. In diabetic retinopathy a similar type of exudation has been demonstrated around some of the fine microaneurysms.

PROGNOSIS

From the foregoing it is apparent that the ocular prognosis of angiomas retinae is poor. This is true not only for the first eye but for the second as well, and it will be recalled that the disease is bilateral in some 50 percent of cases. There is no tendency for the tumor to metastasize.

That the prognosis for life is also poor was recognized by Brandt¹⁰ and others before Lindau showed the relationship of the eye disease to general angiomas. Cerebellar cysts are known to produce death in about 25 percent of cases and may do so in a considerably higher percentage since the cerebellar complications can develop after an interval of many years. Pancreatic cysts and multiple tumors in other organs have also been observed repeatedly.

THERAPY

The treatment of angiomas is difficult at best (Elwyn¹¹) and success is possible only when the tumor can be destroyed in its early stages. No single instance of effective treatment of an advanced case has ap-

peared in the literature. In recent years therapy has been limited to electrolysis, diathermy, irradiation with radium (radon seeds), and X-ray irradiation.

It is apparent from the literature that early angiomas growths, whether in the eye or in other structures, respond to X-ray irradiation and diathermy. So far as the retinal tumor is concerned, diathermy would seem to be as effective as X ray but more damaging to the surrounding retina. Success with diathermy has been reported by Kaye,¹² Lewis,¹³ Guyton and McGovern,¹⁴ and others.

Moore¹⁵ reported successful results with two patients in whom radon seeds had been sutured to the sclera over the site of the tumor. In the first case there was no evidence of the tumor mass at the end of six months and the vessels originally supplying the growth were completely obliterated. In the second case the growths were "scarred up completely" at the end of three months.

X-RAY IRRADIATION

Although X-ray irradiation of advanced angiomas has been uniformly unsuccessful, there have been a number of reports of at least temporarily successful results with early cases. Unfortunately the postirradiation observation periods in these cases have been too short (the longest only three years) to warrant the drawing of any conclusions as to the duration of the derived benefit.

Craig, Wagener, and Kernohan¹⁶ reported a patient to whom they gave three courses of X ray. Three years later the large vessels leading to the mass persisted, but the angioma itself seemed to consist of scar tissue associated with atrophy and a degenerated condition of the surrounding retina. The vision of the eye at this time was 6/4.

In 1940, Cordes and Hogan¹⁷ reported the treatment of a fairly early stage of von Hippel's disease with 1,200 r. A year later the vision was still 20/30. The vessels seemed unchanged, but the exudate had markedly decreased and the tumor was much smaller and flatter. Three and a half years after ir-

radiation⁷ the vascular sacculation and tortuosity had receded but the veins remained enlarged. All signs of exudate had disappeared, the tumor mass was still elevated but smaller than before treatment, and the vision was still 20/30. Neurologic examination at this time was negative except for a positive Romberg sign.

In 1942, Ballantyne¹⁸ treated a case of angiomas retinæ over a three-week period with 4,750 r divided into 14 treatments. Five months later there was marked diminution in the size of the vessels. One year after irradiation the eye showed the effects of X-ray therapy—loss of eyelashes, depigmentation of the skin of the lids, telangiectasis of the lids and bulbar conjunctiva, closure of the punctum, and general rigidity of the lids. Two years after the X-ray therapy there was an extensive intraocular hemorrhage which made enucleation necessary.

The report of Craig and Horrax¹⁹ provided further evidence of the sensitivity of these angiomatic tumors to X-ray therapy. These observers treated a family in which three members had hemangioblastomatous growths: two showed cerebellar involvement and the third spinal cord involvement. Since operative removal of the cord lesion was impossible, the condition was treated successfully with deep roentgen therapy. In their report they referred to an earlier case treated in this way which had regained perfectly normal cord function and had retained it over a 10-year observation period.

Hirschfeld²⁰ reported a case of von Hippel-Lindau's disease in which there was advanced involvement of the medulla and of the retina of one eye. The patient was given a total of 1,475 r directed at the medulla and recovered completely from general brain stem symptoms.

In 1941, Cordes and Dickson⁷ reported a case of angiomas retinæ in a Puerto Rican girl (K. M.); both of her eyes were involved, the right to an advanced degree, the left only moderately. Each eye was given 1,800 r. Two years after irradiation the early

lesion in the left eye showed improvement; the tumor had disappeared and a vision of 20/20 had been retained. During this two-year period, the right eye with the more advanced process became progressively worse until there was complete detachment of the retina, gliosis, and amaurosis.

In February, 1951, M. V., a young Puerto Rican woman, aged 24 years, was seen by one of us at the San Francisco City Hospital and her condition was diagnosed as a case of von Hippel-Lindau's disease. She had bilateral ocular and cerebellar involvement. Investigation of her family history revealed a total of seven members, in the course of three generations on the father's side of the family, with a history of angiomas, either von Hippel's disease or von Hippel-Lindau's syndrome. It was learned that one of these affected relatives, an older sister, married and had four children, was the former patient, K. M., who had received X-ray therapy for angiomas retinæ at our hands in 1941.

It is with the examination of this patient at this time, 11 years after radiation, that the present report is chiefly concerned.

OBSERVATION OF A CASE OVER AN 11-YEAR PERIOD

(December, 1940, to January, 1952)

RÉSUMÉ OF FINDINGS 1940-1942 (previously reported⁷)

On December 20, 1940, K. M., a Puerto Rican girl, aged 14 years, was examined at the University of California Medical Center Eye Clinic because poor vision in her right eye was discovered during a routine school examination. (In March, 1937, she had been seen in this clinic because of "white spots" on the conjunctiva. These were diagnosed as xerosis of the conjunctiva and responded to vitamin therapy.)

Family history. The father, a Puerto Rican, had died of a brain tumor three years previously at 35 years of age. On two occasions, first in 1932 and then in 1934, he

had been operated on for decompression and removal of a cerebellar neoplasm which was diagnosed as angiomatous cyst of the cerebellum. Fundus changes were compatible with increased intracranial pressure.

The paternal grandfather died "quite young" and had been blind for nine months before death.

The mother's family history was negative.

Four sisters, aged 4, 11, 13,* and 16 years, and two brothers, aged 9 and 12, were living and well. Examination of the fundi of all the siblings failed to reveal any abnormalities.

The general physical examination was negative.

Ophthalmic examination. RIGHT EYE. Vision: Light perception; unimproved by lenses. Exotropia. Vitreous hazy. Disc outline almost indistinguishable because of edema and a grayish-white streak extending superiorly to a semisolid-appearing detachment of the retina. The detached retina involved the entire upper periphery and was elevated between five and six diopters.

The inferior nasal vessels were dilated and their outlines became lost in a raised, cherry-red nodule about two disc diameters from the disc margin. The nodule measured three quarters of a disc diameter. The vessels emerging from the distal side of this mass were much reduced in size and were tortuous; farther out along their course there were two other smaller reddish nodules into which both the artery and vein could be seen to enter. Superficial, soft white exudates obscured macular details.

Intraocular pressure was 16.5 mm. Hg (Schiotz).

LEFT EYE. Vision: 20/20. Media clear and disc normal. A branch of the inferior temporal vein was dilated through its entire course to approximately twice its normal diameter. In the extreme periphery this vessel became lost in a reddish-yellow elevated mass one

disc diameter in size. The artery leading to this mass was less dilated than the vein. There was one small, sharply defined area of exudate near the inferior nasal vein in the midperiphery of the retina. The intraocular pressure was 16.0 mm. Hg (Schiotz).

Diagnosis. Well-advanced angiomatosis retinae of the right eye with an early lesion of the same nature in the left.

Treatment. A course of X-ray irradiation was given between February 18 and March 5, 1941. Each eye received 1,800 r.

In the published description of this case abstracted above, the findings on December 15, 1942, 22 months after radiation, were the last data reported. At this time the right eye showed a more extensive detachment of the retina and an increase in the amount of gliosis. The intraocular pressure was 30 mm. Hg (Schiotz). The lesion in the left eye was smaller, flatter, and whiter than it was before irradiation, as though scarring had taken place.

FINDINGS, 1943 (not previously reported)

On July 15, 1943, the patient was examined again. The right eye appeared not to have changed since the previous examination, but the lesion in the left eye seemed a little larger and more elevated. From August 13 to August 25, 1943, two and a half years after the original roentgen therapy had been applied, a course of X ray totaling 2,000 r was given to the left eye.

On October 11, 1943, there was no apparent change except that the tension of the right eye had risen to 40 mm. Hg (Schiotz).

The patient failed to keep her next appointment and investigation revealed that she had moved and left no forwarding address. She was not seen by us until March, 1951, when she was examined in connection with her sister's illness (see above).

Findings on January 11, 1952, 11 years after first X-ray irradiation

RIGHT EYE. Amaurotic. Intraocular pressure: 50 mm. Hg (Schiotz). Exotropia.

* This was M. V. who subsequently developed von Hippel-Lindau's disease, was seen by one of us in 1951, and was the means of our rediscovery of K. M.

Deep anterior chamber. No congestion. Mature cataract.

LEFT EYE. Vision: 20/20. Intraocular pressure: 20 mm. Hg (Schiotz). External and slitlamp examinations negative; no sign of lens opacification. Media clear; disc and macula normal. Neither the vessels nor the angiomatous mass appeared to have changed since the examination of October, 1943. The small patch of exudate previously observed inferonasal to the disc had disappeared.

One disc diameter superotemporal to the old mass was a new lesion: a small, round, grayish-pink mass, one-eighth disc diameter in size and slightly elevated. The mass was fed by a branch of the inferior temporal artery and drained by a branch of the inferior temporal vein. These vessels were normal in size and configuration. There was a small patch of exudate between the inferior vessels but the remainder of the retina was negative.

The general physical examination at this time was negative.

The patient will be kept under observation and the advisability of further radiation for the new lesion will be weighed.

SUMMARY AND CONCLUSIONS

1. Angiomatosis retinae (von Hippel's disease) is a rare, progressive disease characterized by a vascular tumor which in its late stage is marked by gross enlargement of the

vessels leading to it, massive detachment of the retina, atrophy of the disc, and amaurosis; it is frequently associated with angiomatosis and cystic lesions of the central nervous system and viscera (von Hippel-Lindau syndrome).

2. Both eyes of a case with an early lesion in the left eye and a well-advanced lesion in the right eye were treated with 1,800 r; two years later the left eye was exposed to an additional 2,000 r. Eleven years after the first course of X-ray irradiation the well-advanced lesion of the amaurotic right eye remained unchanged; the lesion in the left eye showed atrophy and scarring but no evidence of progression or of lens opacification, and vision was still 20/20.

3. Although the tumor in the left eye had responded to radiation therapy, there was no change in the enlarged vessels leading to it.

4. A small new angiomatous growth, not present when the patient was seen nine years earlier, had developed in the left eye.

5. The results of this 11-year follow-up, which was eight years longer than any other postirradiation observation period on record, confirmed previously recorded experience that treatment of angiomatosis retinae with X-ray irradiation is of no avail in advanced cases but may be successful in early cases.

384 Post Street (8).

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EPIDEMIC KERATOCONJUNCTIVITIS

A STUDY OF A SMALL EPIDEMIC

T. AIDAN COCKBURN,* M.D., AND H. NITOWSKY,* M.D.

Greeley, Colorado

T. ROBISON,† M.D.

Kansas City, Kansas

AND

F. S. CHEEVER,‡ M.D.

Pittsburgh, Pennsylvania

Epidemic keratoconjunctivitis occurred in large scale epidemics before and during the war years,¹⁻³ but since then has been rarely reported. This paper describes a small epidemic in detail and draws attention to the fact that numerous other small outbreaks have come to our attention. Apparently the disease is still present in many places. Serologic studies in a few cases failed to demonstrate any connection between the cases and the EK virus of Sanders and St. Louis encephalitis virus.

The causal virus was claimed to have been isolated by Sanders and his associates,⁴ in 1942, and evidence in support of the identity of this virus was that neutralizing antibodies in high titer persisting for at least two

months could be demonstrated in the convalescent sera of patients. In some instances, a rising titer with a two-or-three-logarithmic increase was found in paired acute-convalescent sera 17 to 34 days apart.

In the later epidemic in New York,⁵ sera from all convalescent cases six to 10 weeks after the onset of illness and 40 percent of cases tested five months after onset showed definite neutralization against the EK virus.

It is well known that herpes virus produces a clinical picture of the disease undistinguishable from the epidemic type, although no one has yet shown that the herpes virus can cause epidemics on the scale of those occurring in the shipyards and elsewhere.

Sanders and others found that the EK virus was not neutralized by antiherpes serum,⁴ but Maumenee and co-workers differed from this,⁶ stating that there is marked similarity between the herpes virus and the EK virus in both the clinical picture they produce and in their immunologic reactions.

* Encephalitis Investigations Unit, Communicable Disease Center, Department of Health, Education and Welfare.

† Department of Ophthalmology, Medical School, University of Kansas.

‡ University of Pittsburgh Graduate School of Public Health.

Ruchman⁶ and Cheever⁷ found a close immunologic relationship between the EK virus and the St. Louis encephalitis virus. These two viruses could not be differentiated by the mouse intracerebral neutralization test, and the only difference was that the EK virus was more pathogenic for rabbits.

There is obviously some confusion as to the nature of the etiologic agent and, to clarify this, an attempt was made to obtain fresh isolation of the virus, with the assistance of ophthalmologists in Colorado, Missouri, Kansas, and Iowa. Although six epidemics in the area as well as a number farther afield were reported, these were only recognized in retrospect, no acute cases were forthcoming and only serologic studies could be made. The transmission of infection in all six outbreaks in the four-state area was associated with eye clinics, but in only one instance was the recording of the clinical and laboratory data complete and exact enough to allow for a reconstruction of events.

This epidemic had been recognized in June, 1951, and an attempt at this reconstruction was made in this one instance about six months later. The eye clinic concerned was a large one employing nine ophthalmologists and treating all forms of eye disorder.

Study of the records revealed that the cases had not been infected simultaneously in one episode as thought at the time, but that transmission from case to case had taken place over a period of many weeks. The long duration of symptoms had led to an accumulation of cases which, when recognized, gave a superficial appearance of an explosive outbreak.

CLINICAL DESCRIPTION OF CASES

All nine patients who developed epidemic keratoconjunctivitis were attending the clinic for treatment and observation of glaucoma. In seven of the cases, the onset of conjunctivitis was sudden, but in two instances the infections were mild in nature for the first two days before the commencement of the severe inflammations.

TABLE 1
DATA ON CASES OF EPIDEMIC
KERATOCONJUNCTIVITIS

Patient	Appearance of Opacities after Onset (in days)	Duration of Symptoms (in days)
E. G.	No opacities	17
L. J.	7	11
C. J.	7	11
D. H.	2	12
B. M.	14	50
F. B.	14	15
J. W.	35	29
C. H.	14	22
A. W.	11	26
Averages	13.0	21.4

Symptoms varied from marked discomfort to severe pain. Inflammation was limited to one eye with intense infection of the conjunctiva and some chemosis. There was little or no purulent discharge, although most of the patients stated that their eyes watered a little. The corresponding preauricular glands were enlarged, though patients did not appear to have had much discomfort from this. Membrane formation developed in some cases on the conjunctiva.

Cultures and smears showed no abnormal micro-organisms. When smears were made the predominant cells were monocytes; a scraping from one patient (C. H.) showed numerous eosinophils. No inclusion bodies were seen in scrapings. The average duration of the acute symptoms was about three weeks (table 1).

Subepithelial opacities typical of those described in other epidemics of epidemic keratoconjunctivitis were found in eight of the nine cases, the only one not developing them being the first case (E. G.). The time of appearance of these is given in Table 1.

EPIDEMIOLOGY

On investigation it was found that the patients who had developed epidemic keratoconjunctivitis were limited to those attending the clinic for glaucoma and that patients with other ailments were not affected. In 1951 there were 5,176 patients treated for all

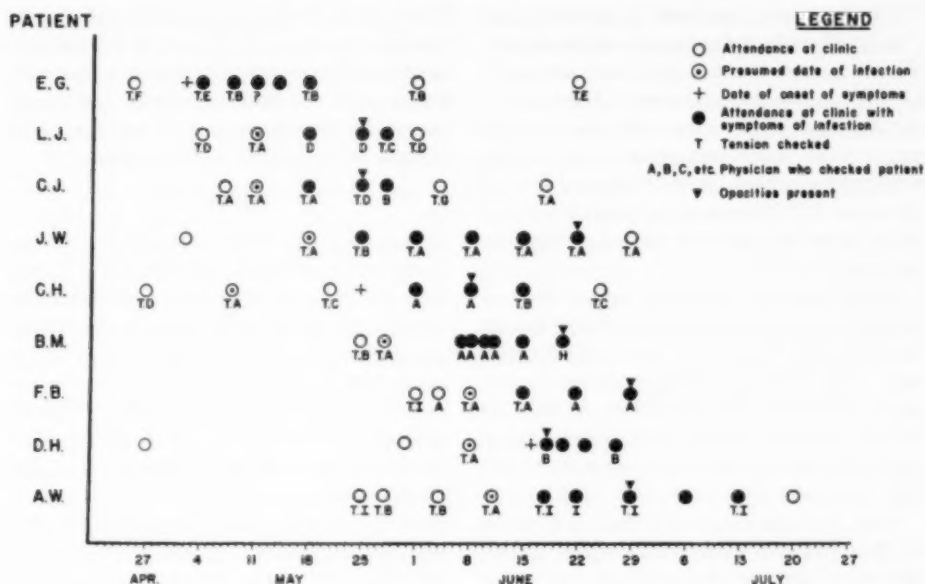


Chart 1 (Cockburn, Nitowsky, Robison, and Cheever). Infectious keratoconjunctivitis in patients attending a glaucoma clinic.

types of eye conditions, the attendances in May, June, and July being 467, 504, and 473, respectively. In these months the average number of tension checks for glaucomatous patients was about 175 per month. In the two-month period under study when patients were being infected, approximately 40 patients with glaucoma were attending, and nine of these became ill, an attack rate of 23.5 percent.

The nine patients with the infection had been attending the clinic for some time, for years in some instances, before the appearance of the disease. Since no cases appeared among the numerous patients examined for other diseases, it was likely that infection had taken place during the examination for glaucoma.

Examination of the procedures used revealed a number of possible mechanisms of infection, such as the fingers of the physicians, the eye dropper, various instruments, towels, and the tonometer used for measur-

ing the intraocular pressure.

Only this tonometer was considered as being the likely vehicle of transmission, for the remainder were used in common for all patients with or without glaucoma, and the latter did not become infected. This tonometer was used for all patients with glaucoma and was sterilized after use by swabbing with alcohol.

The dates of attendance together with information on the physicians making the examination, the use of the tonometer, appearance of symptoms, and the calculated time of infection are shown in Chart 1. The day when each patient was presumed to be infected was calculated by allowing for an incubation period of about five to 10 days and seeing how the days of attendance at the clinic fitted with this.

Scrutiny of Chart 1 will show that on each day that a patient was presumed to have been infected, another patient with symptoms of keratoconjunctivitis had attended;

and that not only had both the infective and presumably infected patients been tested with the tonometer, but had also been examined by only one of the physicians (Physician A on the chart). No other physician of the nine in the clinic was recorded as having examined a patient on the presumed date of infection. Unfortunately, it is not known in what order the patients were examined on each day.

There are two instances where the recorded notes in the patients' charts are incomplete: On May 11th, when patients L. J. and C. J. were presumably infected, they were examined by Physician A but, although infective patient E. G. was present, it is not recorded which physician examined her.

Also, with patient C. H. there is a choice of two possible dates of infection, giving alternative incubation periods of four or 17 days. If the shorter period of time is used, then on the day of attendance no infective patient was present; but if the longer one is accepted, then the patient was examined by Physician A at a time when infective patient E. G. was present. It is not recorded that Physician A examined patient E. G., although it is understood that this quite possibly did happen.

The nature of the epidemic and the possi-

bility of the tonometer spreading the infection was recognized late in June when five patients were attending at the same time with the disease. Further infections were prevented by the adoption of a more efficient method of sterilizing the tonometer.

SEROLOGY

Sera were obtained from four of the patients in the outbreak (epidemic No. 1) and from five patients in a similar outbreak occurring in another eye clinic in November and December, 1951 (epidemic 2). All patients had the classical combination of signs—conjunctivitis without purulent discharge, enlarged pre-auricular glands, absence of pathogenic bacteria, and subepithelial opacities after the appearance of the acute phase of the illness. The sera were tested for neutralizing antibodies against St. Louis encephalitis and epidemic keratoconjunctivitis (Sanders strain) viruses.

Neutralization tests against the viruses of St. Louis encephalitis (Webster strain) and of epidemic keratoconjunctivitis (Sanders strain) were carried out using undiluted serum and decimal dilutions of virus according to the method recommended by the Neurotropic Disease Commission as quoted by Paul.⁸ The convalescent serum specimens which arrived in the laboratory in a liquid

TABLE 2
CONVALESCENT SERA FROM PATIENTS WITH EPIDEMIC KERATOCONJUNCTIVITIS TESTED FOR
NEUTRALIZING ANTIBODIES AGAINST THE ST. LOUIS ENCEPHALITIS
AND THE SANDERS EK VIRUSES

Epidemic	Patient	Corneal Opacities Present	Collection of Sera after Onset of Illness (in days)	Virus Tested	
				St. Louis Encephalitis (Webster)*	Sanders EK*
I	F. B.	+	328	<10	<10
	D. H.	+	333	<10	<10
	C. H.	+	344	<10	<10
	A. W.	+	330	<10	<10
II	W. E. K.	+	63	<10	<10
	M. R.	+	105	125	<10
	V. K.	Not examined	34	<10	<10
	H. E. V.	Not examined	109	<10	<10
	H. E. B.	+	93	<10	10

* Neutralization index.

state were frozen promptly and kept at -20°C . until tested. These sera were not inactivated prior to testing. Normal horse serum inactivated at 56°C . for 30 minutes was employed as a control serum.

Tenfold dilutions of a 20-percent infected mouse-brain suspension were made in 0.4-percent bovine albumen broth. Equal amounts (usually 0.2 cc.) of the virus dilutions and undiluted serum were mixed and incubated in a 37°C . water bath for two hours. Immediately after incubation the serum-virus mixtures were placed in an ice water bath and held there until inoculated into mice. Six three- to four-week-old mice were inoculated per dilution, using the standard inoculum of 0.03 ml. Neutralization indices were calculated in the usual manner.

The results of the tests are given in Table 2. It will be seen that all were negative except for one positive against St. Louis encephalitis virus. This one positive is not significant, for serum surveys in this area show that up to 20 percent of the population may have these antibodies,⁹ and one positive out of 10 could well happen by chance.

DISCUSSION

It is apparent that epidemic keratoconjunctivitis is still appearing in epidemic fashion, although the epidemics are much smaller than during the war years, and all six notified to us were centered around eye clinics. The outbreak reported in this paper demonstrates a method by which the virus can be maintained permanently and in a form that might well escape notice until events provide for a more widespread infection.

The acute phase of the disease may last for several weeks and the likelihood of infected cases wandering from clinic to clinic during the infective acute stage or incubation period and spreading infection wherever circumstances are favorable provides a real danger to ophthalmologists and their patients.

A particular hazard arises in the large clinics, to which patients are sent by ophthalmologists for special consultations, for

should infection be transmitted at such a central point, secondary foci might appear in smaller clinics throughout the country.

In addition, several hundreds of cases of acute conjunctivitis were discovered that clinically were indistinguishable from epidemic keratoconjunctivitis except that opacities failed to develop in the cornea. The diagnoses of these cases pose a difficult problem for, in past epidemics, many apparently genuine cases failed to produce opacities. It is not known if these are examples of epidemic keratoconjunctivitis without opacities or caused by some as yet unidentified virus. Further viral studies on these cases are urgently required.

The findings of the present study would suggest that St. Louis encephalitis virus was not involved in the cases of epidemic keratoconjunctivitis found in the study area. Neutralizing antibodies against this virus can be readily demonstrated in a case of St. Louis encephalitis by the end of two months, and their absence except in one instance in the present series of cases can be considered significant. The one positive serologic test is of little significance since it is likely to happen by chance in testing any group of 10 sera from persons in the Midwest.

The failure to demonstrate antibodies against the Sanders EK virus is of less significance, since less is known about how the antibodies against these viruses fluctuate during and after a human infection. However, the studies that have been reported state that high titer antibodies against the EK virus can be found up to 10,000 neutralizing doses two or three months after the onset of the disease^{1,2,4} and, if the present cases had been caused by this virus, antibodies should have been found at least in Epidemic 2. It is possible that there is more than one epidemic keratoconjunctivitis virus and that the cases described in this paper were caused by another such virus not yet isolated.

SUMMARY

1. Epidemic keratoconjunctivitis is still

occurring, and six small epidemics, all centered around eye clinics, were found.

2. In one epidemic, the infection was maintained in patients with glaucoma for many weeks by transmission from patient to

patient, probably by a tonometer.

3. Serologic studies showed no relation between the disease in two epidemics and St. Louis encephalitis and the Sanders EK virus.

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SURGICAL CORRECTION OF SPASTIC SENILE ENTROPION: A NEW METHOD*

DANIEL B. KIRBY, M.D.
New York

The multiplicity of procedures and methods for the relief and cure of spastic senile entropion indicates the difficulty of the condition. The unsatisfactory results which are obtained when any one method or operation is applied routinely prove that the patient who has spastic senile entropion must be treated as an individual and the appropriate treatment and surgery applied.

It has been my observation that in many of the patients in the senile age group who suffer from spastic entropion, there is present also a flaccidity and apparent elongation and relaxation of the lower lid which is due undoubtedly to degeneration of the previously dense elastic and fibrous tissue ele-

ments. It is definitely not the redundancy of skin alone which is at fault. In the presence of irritation or inflammation, entropion may develop through spasm or even through the normal action of the orbicularis muscle.

By removal of the irritation or a cure of the inflammation and by shortening and tensing the lower lid, the condition of so-called spastic senile entropion has been overcome and cured in all of the cases in which the procedure to be described has been indicated and applied. It is to be admitted that further degeneration may occur and that, if degeneration is coupled with irritation or inflammation, the entropion may well recur.

BACKGROUND

It is interesting to describe the development of the recognition of the principle and

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the application of the surgical procedure. I was associated with John Wheeler and knew of his transplantation of fibers of the orbicularis muscle for the correction of spastic senile entropion. I had also seen him use an operative procedure to shorten and narrow the palpebral fissure for relief of the bulbar exposure due to proptosis in cases of exophthalmic thyroid disorders. I had used the Kuhnt-Szymanowski¹ operation for relief of the great flaccidity of the lower lid in cases of seventh cranial nerve paralysis. I found that the latter condition could just as well be relieved by a much simpler shortening and tensing of the lower lid.

After recognition of the principle of senile degeneration as the cause of the elongation and flaccidity of the lower lid, it was simple to postulate that the orbicularis, instead of causing the lower lid to hug and conform to the convexity of the globe, might well roll its margin inward. I applied a simple method of resecting and advancing the deep lateral tissues of the lower lid in such cases and succeeded in the correction of the spastic senile entropion.

The dissection is similar to that used by Wheeler in his preparation of the lower lid in his exophthalmic cases, but the palpebral fissure is not shortened or narrowed.

IDEAL OPERATION FOR RELIEF OF ENTROPION

Spaeth² was right when he postulated the necessary factors for an operation for entropion:

1. It must relieve the faulty position of the cilia.
2. It must prevent the subsequent recurrence of the faulty position.
3. It must do this with the least amount of disfigurement.

It will be shown that this new procedure conforms to these postulates.

LIMITATION OF DISCUSSION

The various types of entropion must first be differentiated. Those due to cicatrices, to

contraction, or to deformity, whether developmental or acquired, will not be discussed here. The condition of spastic entropion associated with psychosomatic disorders or with various forms of irritation and inflammation of the ocular structures will not be considered.

This paper is limited to the condition known as spastic senile entropion, to the procedures which have been or may be applied to it, and to this new procedure which has been successfully used.

SPASM OF THE ORBICULARIS

Meek³ and McCool⁴ and others are in accord that there is a definite spastic action of the orbicularis as a basic factor in the production of the entropion. Meek analyzed McCool's ideas as follows:

He stated that the palpebral fibers of the orbicularis oculi muscle form arcs, the concavity of which is pointed in two different directions. One type of curvature surrounds the palpebral fissure and directs its concavity toward the fissure; the other type of curvature is caused by the fibers being molded to the eyeball with the tarsus. The concavity of this type is directed toward the eyeball. With deficient support of the free border of the eyelid and an excess of skin on the lower lid, contraction of the palpebral fibers of the orbicularis oculi muscle takes place, and what was formerly an arc becomes the chord of an arc. The fibers exert a double action, narrowing the palpebral fissure and pressing the tarsus against the eyeball. Either action may cause entropion.

This pressure against the eyeball is the more important because the lower lid is in perfect contact with the eyeball only so long as the eyeball gives proper support. When there is enophthalmos, an empty socket, a small eyeball or lack of orbit fat, as is seen in senile persons with sunken eyes, the free edge of the lid receives insufficient support posteriorly and the tarsus may bend in or out, giving rise to entropion or ectropion. The character of the skin is important because a large amount of loose, wrinkled, and readily displaceable skin contributes to the formation of the entropion. A healthy, firm skin with good tone will not readily give way.

It is important to note that many have written of the redundancy of the skin in those cases, but none have described the flaccidity and elongation of the previously dense elastic and fibrous tissue elements of the lower lid.

I agree with the other points in the discussion, but would add that it may only be the normal or ordinary action of the orbicularis that may, under the conditions given, produce the entropion. I agree also that the condition when once formed may appear to be due to spastic muscular contraction.

My impression may be repeated here, that it is the flaccidity and elongation of previously dense fibrous and elastic tissues of the lower lid in the condition of senile degeneration which permits the normal or the spastic action of the orbicularis to produce the entropion.

LITERATURE ON CORRECTION OF SPASTIC SENILE ENTROPION

Celsus-Hotz procedure. Perhaps the oldest procedure is that of Celsus.⁵ It was modified by Hotz.⁶ They excised lower lid skin and some orbicularis muscle fibers, then united the edges of the skin with sutures, thus producing traction on the lid margin.

Temporizing methods of treatment. These are valuable since the relief of irritation or the treatment of inflammation may effect a cure. The use of various adhesives, collodion, tapes such as scotch or waterproof zinc oxide adhesive tape, afford temporary relief. I see no reason for the removal of cilia in any ordinary cases of spastic senile entropion.

Injection of procaine and alcohol. Many surgeons have used the temporary expedient of procaine, while others, notably Hughes,⁷ have used alcohol injections into the muscle and nerve fibers.

Benedict⁸ thought that the blepharospasm was due to irritation in the region of the trigeminus or to essential irritation of the central nervous system. He advocated injection of alcohol for the short duration therapy. He also tried section of the peripheral branches of the facial nerve. He preferred the alcohol injection and found that the best place to inject it was in the region of the parotid plexus.

Section of seventh cranial nerve branches. This has been done, the exposure being made

by dissection just anterior to the ear, the nerve bundles being found in the anterior border of the parotid gland. I would not recommend this procedure for spastic senile entropion.

Traction by sutures. Sutures have been used for traction upon the lid and its margins. The most widely copied method for the correction of spastic entropion is that of Gaillard.⁹ Curved needles are inserted two to three mm. below the lid margin to run beneath the skin and emerge near the inferior orbital margin. They are tied over gauze or rubber to help produce tension and even eversion.

Snellen¹⁰ passed the sutures from the conjunctival surface near the lower cul-de-sac, through the tissues of the lid to emerge near the margin just below the line of lashes. Tying the sutures everted the lid margin. If the sutures are left in for quite a period of time, they induce cicatricial bands which by their contraction help in the permanent cure of the entropion.

MacDonald¹¹ used a Michel metal clip on the lower lid skin beyond the outer canthus so that the orbicularis muscle contraction may not invert the lid. He reported that only one of his cases required surgical treatment later.

Cautery puncture. Ziegler¹² found that contraction of the lid tissues could be induced by multiple cautery punctures made through the lower lid skin. Wheeler¹³ used this method for quite a while, urging that a second line of punctures be made below the first, thus inducing vertical rather than lateral cicatricial band contraction for the more efficient correction of the condition by this method.

Graefe operation. Graefe¹⁴ and others recognized, as did Celsus and Hotz before them, the redundancy and flaccidity of the tissues of the skin of the lower lid in cases of spastic senile entropion and reiterated the principle of resection of the skin for its correction. None of them brought out the principle of the degeneration of the dense fibrous

and elastic tissue being the particular reason for the development of the spastic senile entropion. They all laid emphasis on the relaxed skin and the orbicularis spasm.

Meller's technique. Meller¹⁸ practiced the Graefe operation. He excised a triangular piece of skin of the lower lid. His first incision was three cm. long and placed three mm. below the lid margin. Two other incisions ran downward from either side of the central area of the first incisions to form a triangle of skin which was excised. The lateral skin was slightly undermined and the edges joined.

Imre's technique. Imre¹⁶ modified the Celsus-Hotz procedure by adding the excision of a triangular piece of skin extending down from beneath the lateral canthus.

Duverger's technique. Duverger¹⁷ excised an elliptical piece of skin from below the lid margin and added the excision of a triangular area beneath the lateral canthus, but did not join the areas as did Imre.

Blaskovics's technique. Blaskovics¹⁸ made a more extensive dissection and undermining than Imre did. He placed the excision of the triangular area of skin further temporalward.

Poulard and Poshikov. Poulard¹⁹ and Poshikov²⁰ first did a lateral canthotomy, then they sectioned the lateral canthal ligament. They excised four mm. of the skin of the lid margins of the lower lid and two mm. of the upper lid and joined the cut edges, thus correcting the entropion, but needlessly shortening and narrowing the palpebral fissure.

Lateral canthoplasty. Vogt²¹ applied a different principle, that of aiming to turn the lower tarsal plate into a better position by dividing the lateral canthus freely, carrying the incision to the lateral wall of the orbit.

He then passed a suture through the skin of the upper lid to emerge about the middle of the cut surface from whence it passed through the conjunctival surface of the lower lid, finally coming out about the middle of the lower lid cut. Tying the suture everted the

tarsal plate as well as the lower lid.

Tarsectomy. Kuhnt as reported by Meek³ practiced lateral tarsectomy to relieve a deformed position of the tarsus. This would be in order in certain cases of cicatricial entropion, but would have no place in the correction of spastic senile entropion.

Transplantation of the orbicularis muscle fibers. Wheeler²² initiated the principle of transplantation of the orbicularis for the correction of spastic senile entropion. Hughes²³ and Meek³ modified it in practice.

Wheeler's first technique consisted in the dissection of two opposing bands of orbicularis muscle four to five mm. wide from a division in the central area of the lower lid, then the overlapping of these muscle bands by a mattress suture.

In his second technique he dissected up a band on the orbicularis muscle, left it fixed at the median position, freed it in the lateral area, then stretched or tensed it and brought it upward and outward and over the lateral orbital margin, to be attached to the periosteum slightly superior and lateral to the orbital tubercle.

Hughes made a dissection in every way similar to that of Wheeler's second technique, but transplanted the strip of muscle down and laterally.

Meek dissected up two tapered strips of orbicularis from the lateral ends, leaving the central area of each strip attached to the underlying tissues. He then transplanted the tips of each strip downward, the one nasally, the other temporally, suturing them loosely to the anterior surface of the inferior orbital margin. Meek later decided that usually it is necessary to use only one of these flaps the correction for so obtained was ample.

Sanchez-Bulnes,²⁴ after analyzing the manner in which the orbicularis muscle acts in the formation of the senile spastic entropion, utilized these fibers by inverting them. He placed a bundle of fibers from the pretarsal portion of the muscle behind the tarsus, through a hole made in the orbital aponeurosis.



Fig. 1 (Kirby). Redundancy, flaccidity, and increased length of the lower lid in a case of spastic senile entropion.

PRINCIPLE OF MY NEW METHOD OF CORRECTION OF SPASTIC SENILE ENTROPION

My observations in most cases of spastic senile entropion, over a period of 10 or more years, have definitely indicated that, when the spastic or normal contraction of the orbicularis is relieved by any method, not only the skin but also the deeper lid tissues appear to be flaccid, flabby, redundant, and that the length of lid tissue between the fixed points of the medial and lateral canthi is too great. Because of this condition, normal or spastic contraction of the orbicularis tends to flip the lower lid inward, thus producing the condition of spastic senile entropion.

When the orbicularis is paralyzed, such a lid tends to sag and to evert. The intorted lower lid of spastic senile entropion cases, when everted manually and pinched up between the fingers, can be shown to be elongated and unduly relaxed. I have applied these observations in a practical manner and



Fig. 2 (Kirby). Schematic drawing, showing relations of skin, orbicularis deep fasciae, lateral canthal ligament, and lateral orbital margin.



Fig. 3 (Kirby). Initial incisions and excision of the lateral portion of the lower lid margin. The lashes in this area are included in the excision.

have corrected the condition in about 25 cases, in a period of five years or more, by simply resecting and advancing the tissues of the lateral end of the lower lid.

It cannot be argued that the severance of or interference with the few orbicularis fibers involved in the procedure accomplishes the result. Hughes made the same observations in regard to the elongation of the relaxed lid of the senile group. It was natural that he should arrive at the same conclusions that I did, since he had the same training and experience. Hughes²³ corrected the condition by a modified Kuhnt-Szymanowski procedure.

TECHNIQUE

Local infiltration, block anesthesia, or general anesthesia may be used.

The extent of the resection and advancement of the dense tissues of the lower lid is



Fig. 4 (Kirby). Fashioning of the skin to be excised.



Fig. 5 (Kirby). Excision of skin.

determined by the degrees of flaccidity and elongation of the lower lid and also by the degrees of the entropion (fig. 1). An idea of this may be obtained by pinching up the tissues of the lower lid, feeling not so much for the degree of redundancy of skin as for the relaxation of the dense fibrous and elastic tissues of the lid (fig. 2). In general, a change of three to six mm. in length is made.

A rectangular piece of skin on the outer surface of the lower lid is removed from the area directly below the angle of the lateral canthus. The skin incisions extend nasally to the degree determined by conditions present. The piece of skin removed may measure four mm. by five or six mm. in area.

The lid margin epithelium together with the lashes is then removed to a similar extent from the canthal angle nasally (figs. 3, 4, and 5). The conjunctiva is dissected back, but not necessarily removed (fig. 6). Finally

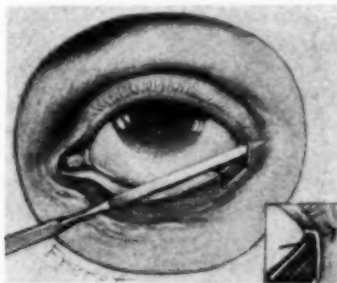


Fig. 7 (Kirby). Correct manner of fashioning the tunnel or sheath into which the tongue of tissue from the lower lid will fit. Thus only the lower lid is shortened and tensed.

the tarsus is severed by a vertical cut through the tarsal ligament temporarily.

These four steps result in the fashioning of a pedunculated tongue of lid tarsal tissue three to four mm. vertically by five to six mm. laterally. Some of the length of this tongue may be sacrificed by resecting a few millimeters from its free border, although this is not necessary or always advisable, since the longer tongue affords a stronger union with the ligament and orbital tissues temporarily.

The tongue of tissue is now transplanted into a sheath prepared for it by slicing with a knife just anterior to the tarsal ligament and periosteum (figs. 7 and 8). Two double-armed 4-0 silk sutures with three-eighths curve needles are passed through the tongue of lid tarsal tissue from the inner surface

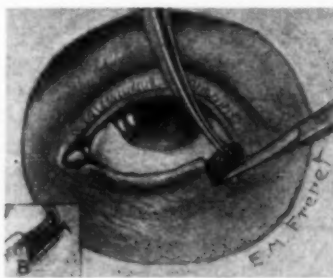
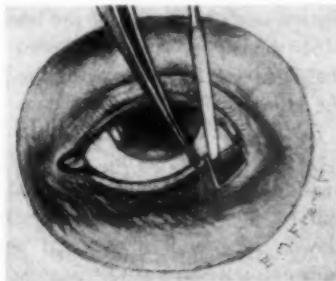


Fig. 6 (Kirby). Splitting and excision of the conjunctiva from the inner surface. (Left) The lower part of the tarsal ligament is then severed from the lateral orbital margin. (Right) Scissors are used to sever the attachment of the tarsus from the lateral canthal ligament and to cut along the lower border, thus forming the tongue of tissue for transplant.



Fig. 8 (Kirby). Incorrect way to fashion the tunnel or sheath. The incision should not be carried higher than the angle of the lateral canthus. Thus shortening and narrowing of the palpebral fissure are avoided.

outward (fig. 9). These are then passed into the dense tissues of the ligament and periorbitum to emerge through the skin temporally and to be tied over rubber plates or buttons (fig. 10). The course of the dissection and sutures is in an arc following the normal curve of the lower lid upward and outward.

COMMENT AND SUGGESTIONS

The tongue of tissue as prepared for transplant should not be traumatized so that its vitality will not be reduced. The inner end of the tongue of lid tissue is carried to the previous outer end of the same. The only effect, therefore, is that of shortening and tensing the lower lid. It is interesting that this is sufficient to correct the entropion

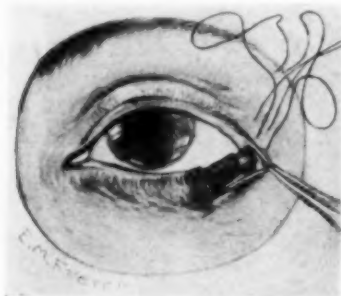


Fig. 9 (Kirby). Two double-armed 4-0 silk sutures are passed through the tongue of lid tissue, then into the preperiosteal tissue sufficiently lateral to the orbital margin, then out through the skin.



Fig. 10 (Kirby). Tongue of tissue from the lower lid advanced into the tunnel or sheath, anchored, and sutures tied. The skin edges are united with 6-0 black-silk sutures.

without further procedure.

It is usually not necessary to resect skin to any greater extent than described. There is no puckering or deformity. There are cases in which the redundant skin, for cosmetic reasons, may be resected, but this is not necessary for the correction of the entropion. Caution is urged in the removal of skin and orbicularis in any case, since permanent eversion may easily develop.

It is important to refer back to Wheeler's use of a similar tongue of lid tissue in the correction of the widened and elongated palpebral fissure of exophthalmos. It is important to note that in my new application of this technique the palpebral fissure is not narrowed or shortened as it was in the Wheeler procedure. Wheeler inserted the tongue of lid tissue into a sheath prepared by dissection and splitting of the lateral portion of the upper eyelid anterior to the canthal ligament, thus advancing the position of the lateral canthal angle.

A further indication for the use of this new procedure. This technique may be used as an additional and desirable method of correction of the flaccidity and elongation of the lower lid found in cases of persistent seventh cranial nerve paralysis.

RESULTS

In the 25 cases in which this procedure has been used over a period of five or more

years, all were successful on the first attempt except three. The latter were not failures, since in the recurrence of the entropion it was noted that there was residual uncorrected lid flaccidity and elongation, and it was possible to remedy this by a second and similar surgical procedure. The balance of the cases remained corrected by the first operation. In some of these, previous palliative and other operative procedures had failed.

DISCUSSION

Senile degenerative flaccidity and elongation of the low lid is disclosed to be the very basis of the development of spastic senile entropion. The actual exciting factor and the spasticity of the orbicularis muscle may be simply coincidental at the particular time that the entropion develops.

The principles of many of the procedures used in the correction of this condition involve *traction* as by tape, sutures, clamps, production of cicatrices, resection of skin and orbicularis, change of position of the tarsus, transplantation, and change of direction of orbicularis muscle. Most of these operations act by the production of *traction* on the lid margin.

I have advocated shortening and tensing of the dense, deeper tissues of the lid, thus correcting the flaccidity and elongation of the degenerated lid tissues of the elderly or senile group of patients in which this condition develops.

It is not my intention to urge the use of this new procedure alone for all of these cases, since other surgeons have been suc-

cessful with the various procedures which have been reviewed. I offer it, however, as an addition to their armamentarium, since it most aptly applies the evident principles of removal of degenerated redundant and flaccid tissues, thereby tensing the lid and correcting the entropion.

I do urge that, when flaccidity, elongation, and relaxation of the lid is found in cases of spastic senile entropion, this new procedure be given precedence for its corrective quality. It fulfills the criteria set up by Spaeth and it has been found effective in cases in which other procedures were unsuccessful.

SUMMARY

A new principle as the cause of spastic senile entropion has been presented—in that it is senile degeneration of elastic and fibrous tissues of the lower lid which produces flaccidity and elongation of the lid and permits the development of spastic senile entropion by the spastic or even by the normal action of the orbicularis upon the slightest irritation or inflammation.

A new procedure, consisting in the resection of the dense tissues of the lower lid and their advancement temporally over the canthal ligament and lateral orbital margin to shorten and tense the lower lid, has resulted in the correction of spastic senile entropion with a great percentage of success.

The procedure may also be used in cases of flaccidity and elongation of the lower lid due to persistent seventh cranial nerve paralysis.

780 Park Avenue (21).

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CATARACTS IN GALACTOSEMIA*

JERRY JOHNSON, M.D.

Maxwell Air Force Base, Alabama

Galactosemia or galactose diabetes is a rare congenital abnormality characterized by a derangement in the metabolism of galactose. Galactose and glucose are the monosaccharides resulting from the breakdown of lactose. The cause of this disorder is obscure but presumably is due to some primary hepatic defect. The onset is in the first weeks of life with considerable variation in severity.

The outstanding features of the syndrome are: cataracts, hepatomegaly, splenomegaly, failure to gain weight, and reducing substance in the urine. Frequently associated phenomena are persistent icterus, anemia, lethargy, absence of deep reflexes, mental retardation, and a familial tendency. The diagnosis may be definitely established by isolation of the phenyl osazone of galactose from the urine.

REVIEW OF LITERATURE

The first case of galactose diabetes was

reported by von Reuss¹ in 1908. His patient was a child who had hepatosplenomegaly and galactosuria. The child died when eight months of age. Autopsy revealed hepatic cirrhosis. The author felt the cirrhosis was due to alcohol, since the child had been fed cognac daily.

Many feel that the first acceptable report of this syndrome was made by Goppert² in 1917. His patient was two and one-half years of age when first seen and had hepatomegaly, retarded growth, and galactosuria. Two siblings had died in the first two months of life with icterus and hepatomegaly. Another sibling, age six years, was known to have hepatomegaly.

Fanconi,³ in 1933, reported a nine-year-old child with mild galactosemia. He was but slightly underdeveloped and his liver was not enlarged. This child and two otherwise normal siblings had zonular cataracts; therefore, this may not be a true example of cataract associated with galactosemia.

In 1935, the first case in American literature was reported by Mason and Turner.⁴ Their original report does not mention cata-

*From The Departments of Ophthalmology and Pediatrics, University of Texas Medical Branch, Galveston, Texas.

TABLE 1
REVIEW OF LITERATURE

Author	Year Reported	Age of Patient	Type of Cataract	Course
Mason and Turner ²⁶	1945	6 mo.	Not reported	Slight improvement Surgically treated
Bruck and Rapoport ⁵	1945	7 wk.	Nuclear	Complete resorption
Goldbloom and Brickman ²²	1946	6 mo.	Lamellar	Slight improvement
	1946	3.5 mo.	"Central anterior opacity"	Slight improvement
Goldstein and Ennis ²³	1948	2.5 mo.	Zonular	Complete resorption at age 4 mo.
Greenman and Rathbun ²⁴	1948	4.5 mo.	Nuclear	Improvement
Ennis ²⁵	1951	6 wk.	Nuclear	Complete resorption
Falls, Lowrey, and Anderson ²⁸	1951	8 wk.	Zonular	Unknown
Reiter and Laskey ²⁷	1952	7 wk.	Zonular	Complete resorption
Langewisch and Bigler ²⁸	1952	7 wk.	Nuclear and lamellar	Improvement
Johnson	1953	3 wk.	Nuclear	Complete resorption
	1953	4 mo.	Cortical	Considerable improvement after 6 mo.
	1953	1 yr.	Nuclear and lamellar	Far advanced—no improvement expected

* Reported by Bruck and Rapoport, 1945.

tracts, but in a personal communication to Bruck and Rapoport they state that their patient did have cataracts, which were treated surgically. The type is not reported.

Bruck and Rapoport⁵ in 1945, described a seven-week-old infant with galactosemia and associated nuclear cataracts. The lenticular opacities resolved completely after a milk-free diet.

With one exception, in all of the cases reported since 1945, cataracts have been present (table 1). The exception is the child cited by Bell and others⁷ in 1950. In this instance diagnosis was established and treatment instituted before the child was two weeks of age. Lenticular opacities may have developed had he not received prompt care. A sibling, a proven case of galactose diabetes, died at the age of eight days, without lenticular involvement.

There have been many reports concerning the metabolic aspects of galactosemia.⁴⁻¹⁰ Of special interest, however, are the reports on the experimental production of galactose cataracts.¹¹⁻²¹

In 1932, Kirby and others¹¹ pointed out that there was a definite toxic effect exerted

by galactose on epithelium of lenses cultured in vitro.

Mitchell and Dodge,¹² in 1935, made the important observation that rats fed on a diet containing 70-percent lactose invariably developed cataracts, the majority of which progressed to maturity. They further noted that the younger the rat the more rapid the onset of lenticular changes and that a higher percentage of the cataracts in younger rats progressed to complete maturity.

Bellows and Chinn¹³ demonstrated in rats that various hypertonic solutions injected intravenously would produce cataracts within a few minutes. They observed that hypertonic solutions of intravenous saline as well as galactose would cause a similar transient opacification of the lenses.

Mitchell felt that the lens capsule and epithelium were injured by galactose, leading to an increased penetration of inorganic ions. Bellows and Rosner¹⁴ reported that there is decreased permeability of the lens capsule caused by galactose. They show that the calcium content of a galactose cataract remains at a normal level until the cataract reaches maturity.

TABLE 2
TYPES OF CATARACTS

Age of Patients	0-2 Months			2-4 Months			Over Four Months		
Type of Cataract	Nu-clear	Cor-tical	Com-bined	Nu-clear	Cor-tical	Com-bined	Nu-clear	Cor-tical	Com-bined
Number of Cases	3	2	1	0	3	0	1	1	1

The chemical changes occurring in galactose cataracts have been studied by a number of investigators. Bellows¹⁷ showed that excessive galactose causes a loss of glutathione, cystine, and vitamin C from the lens. Sali and others¹⁸ found an increase in the total ash content of these lenses. The sodium, calcium, sulfate, and carbonate content is increased but potassium, phosphate, and chloride are decreased.

It is rather remarkable that the experimental aspects of galactose cataracts were known several years before the lesion was observed in a human patient. However, once noted, it has become an integral part of the syndrome.

CASE REPORTS

CASE 1

History. S. J. F., a three-week old white girl, was admitted to the Pediatric Division of The University of Texas Medical Branch

Hospitals on January 2, 1951. The child was born at term on December 11, 1950. The birth weight was seven pounds and two ounces. At the age of five days she developed jaundice, which was present at the time of admission. The infant always had a poor appetite; was very inactive; slept most of the time; rarely cried; and failed to gain weight.

This was the seventh child of healthy, young parents. The first three siblings were normal. The fourth child died when two and one-half months of age of unknown cause. However, it was known that the child had an enlarged liver. The fifth pregnancy resulted in twins, one of which was stillborn. The other died three days after birth. It is not known whether any or all of the last three siblings suffered from galactose diabetes, but the history is suggestive.

Physical examination. The patient was jaundiced and lethargic. She was malnourished, the weight being only six pounds and 10 ounces. The liver was palpable six centimeters below the right costal margin. The spleen was palpable two centimeters below the left costal margin.

Ocular examination. There was an icteric tint to the conjunctiva. Pupils were round, regular, and reacted promptly to light. Extraocular movements were normal. Ophthalmoscopy revealed the retina and disc to be normal and the media to be clear except that the lenses had nuclear opacities. These were very early, being areas of hyperrefractility accentuating the nuclear areas (fig. 1).

Laboratory data. Repeated urinalysis revealed 4+ reducing substance, which was identified as pure galactose.* The blood sugar was 124 mg. percent, one half of which was

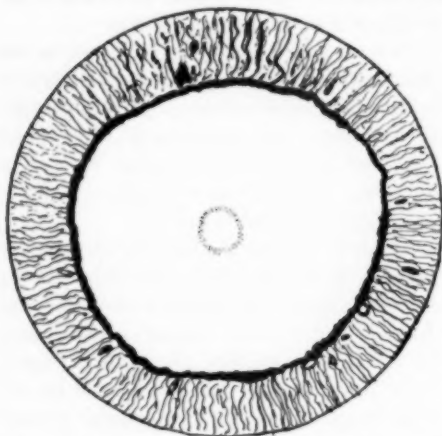


Fig. 1 (Johnson). Drawing illustrating the nuclear lenticular opacification seen in Case 1.

galactose. Oral and intravenous tolerance tests revealed a marked galactose intolerance.

Course. Milk was withdrawn from the diet and a soy-bean formula substituted. On the fifth day of milk-free feedings there was no reducing substance in the urine and the spleen was no longer palpable. Within two weeks the lenticular opacities had cleared completely and the liver was no longer palpable. The child was discharged from the hospital in good condition.

She was readmitted on February 12, 1952, after having been kept on the milk-free soy bean formula during the past year. She was in excellent health. Neither the spleen nor the liver were palpable and both lenses remained perfectly clear of opacification.

CASE 2

History. K. L. W., a four-month-old white girl, was admitted on February 7, 1952. She was born at term on October 10, 1951. Birth weight was nine pounds and seven ounces. The pregnancy and delivery were normal. At the age of one week she became jaundiced but this persisted for only five days. The child had been irritable; had been a feeding problem; had failed to gain weight; had had vomiting and diarrhea; and was referred here with the probable diagnosis of Von Gierke's disease, which had been suggested from liver biopsy. The referring physician had used insulin in low dosage in an effort to control persistent glycosuria. However, each injection of insulin precipitated a hypoglycemic reaction.

The family history revealed that a sister born in 1946 had died at the age of seven weeks. She was known to have had hepatomegaly. A brother born in 1949 remains in excellent health.

Physical examination. The infant was lethargic and malnourished. The weight was nine pounds and 12 ounces. The abdomen

*Chemical determinations performed by A. A. Ormsby, associate professor, Department of Biochemistry, University of Texas Medical Branch.

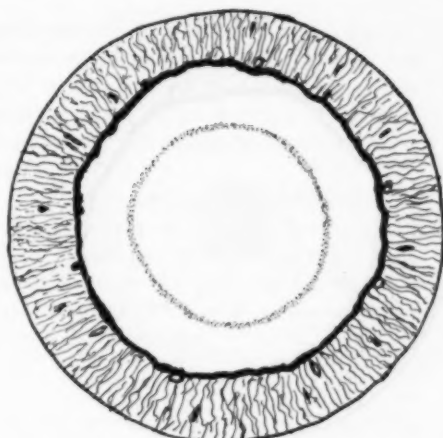


Fig. 2 (Johnson). Drawing illustrating the cortical lenticular opacification noted in Case 2.

was protuberant. The liver was palpated almost down to the level of the umbilicus.

Ocular examination. External examination was negative. The pupils were round and equal and reacted normally to light. Extraocular movements were normal. Ophthalmoscopy revealed bilateral cortical cataracts with clear nuclear areas (fig. 2).

Laboratory data. Urinalysis showed 2+ albumin and 2+ reducing substance, which was identified as galactose. The galactose tolerance test was positive, revealing a sustained elevation of the blood and urine levels of galactose. A liver biopsy proved a moderate hepatic cirrhosis.

Course. The patient was placed on milk-free feedings. On the fifth day the urine was free of all reducing substance and the child was much more alert.

At the time of discharge, on February 23, 1952, the child was much improved. The liver had receded to but four centimeters below the right costal margin. However, there had been no appreciable change in the lenticular opacities.

The patient was reexamined on September 9, 1952. At that time her general status was much improved, although the liver was still

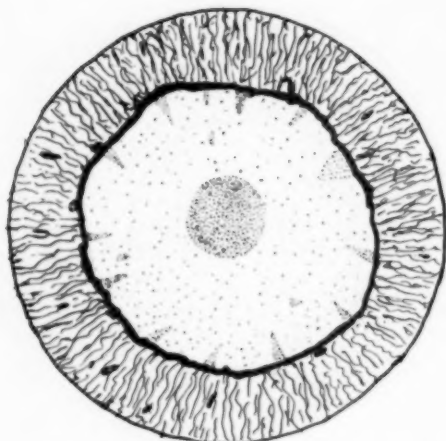


Fig. 3 (Johnson). Drawing illustrating the nuclear and lamellar lenticular opacification noted in Case 3.

palpated at about the same level. The lenticular opacities were markedly improved, there being only a thin line of hyperrefractility in the periphery.

CASE 3

History. W. H., a one-year-old white boy, was admitted on March 31, 1952. Pregnancy and delivery were normal. The birth weight was eight pounds. On the fourth day of life jaundice developed and persisted for six weeks. The baby was breast fed and had nursed well but had failed to gain weight. At six months of age hepatosplenomegaly was found. He had been given repeated blood transfusions and was on a high vitamin intake when admitted to the hospital. This was the only pregnancy and there was no history of familial diseases.

Physical examination. The patient was lethargic and malnourished. The weight was 11 pounds and eight ounces. The abdomen was distended; the liver was palpable at the level of the umbilicus; and the spleen was palpated four centimeters below the left costal margin.

Ocular examination. External examination was normal. The pupils were normal in size and reaction. The extraocular movements

were normal. Ophthalmoscopy revealed bilateral dense white nuclear opacities as well as spoke-shaped peripheral cortical opacities. These lens changes obscured the details of both fundi.

Slitlamp study showed that all layers of these lenses were infiltrated with tiny white opacities, which were closely packed together to form the peripheral cortical or lamellar spokes (fig. 3).

Laboratory data. The urine was consistently positive for reducing substance, which was identified as galactose. Developmental studies showed the child to be at a two-to-three-month level. A pneumoencephalogram revealed marked cortical atrophy of the brain.

Course. The patient was placed on milk-free feeding and discharged from the hospital before any changes could be noted other than an improved alertness. It is not expected that there will be any degree of improvement in the lens opacities or in the patient's overall condition. No follow-up examination has been possible.

DISCUSSION

These three patients with proven galactosemia had three different types of cataracts. One was nuclear; one was cortical; and one patient had both nuclear and cortical opacities. A review of the types of cataracts listed in Tables 1 and 2 shows no definite correlation between the type of lenticular change and the age of the patient. However, from Table 2 it is suggested that nuclear cataracts are more likely to occur in the younger patients. Here we observe that three of the four patients with nuclear cataracts only were two months of age or less.

From Table 1 we note that five of the 13 reported cases of cataracts associated with galactose diabetes have resolved completely on milk-free feedings. The oldest one of these five patients was two and one-half months of age.

It may not be stated dogmatically but one can certainly say that removal of milk from

the diet before the third month of age is imperative for the prevention of irreversible lens changes. This is one of the few conditions in which human milk is probably more harmful than cows' milk in infant feeding, the reason being that human milk has a carbohydrate content of about 7.0 percent as compared with about 4.5 percent carbohydrate content of cows' milk. The carbohydrate of all milk is lactose.

The similarity of the human cataracts to the experimental galactose cataracts has been pointed out by Reiter and Lasky.²⁷ Galactose has been of utmost importance in experimental ophthalmology, because, as is pointed out by Bellows,²⁸ it is the only cataractogenic agent that will consistently and rapidly cause cataracts. The other agents are far less reliable and take much longer in most instances.

The third case in this report showed tiny punctate opacities scattered throughout all layers of the lens and grouped together in condensed masses to form the lamellar portion of the cataracts. This confirms the previously observed fact that the lenticular changes are often composed of such tiny punctate opacities.

In the first two cases presented herein, there is an extremely suggestive history of galactosemia in other members of the sibship. The last patient was an only child. All of the parents were in good health. Perhaps further knowledge regarding this interesting

syndrome will be forthcoming with the generation descended from the patients with these known controlled cases of galactose diabetes. None of the patients in American literature are old enough to have families of their own.

It would be well for all ophthalmologists, when examining an infant with cataracts of uncertain etiology, to insist that an examination of the urine for reducing substances be performed in order that this rare syndrome may not be overlooked.

SUMMARY

1. The literature is reviewed regarding galactose diabetes in human subjects and galactose metabolism in experimental animals.

2. All of the known cases of cataracts associated with galactose diabetes have been reviewed.

3. Case reports of three new cases of galactose diabetes with cataracts are presented. These are infants aged three weeks, four months, and one year. Each child has an entirely different type of cataract.

4. The importance of early diagnosis based on cataracts, hepatosplenomegaly, retarded growth, and the presence of reducing substance in the urine is noted.

5. The essentiality of treatment, by removing milk from the diet, before the third month of life is stressed in order to prevent irreversible lens opacification.

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OPHTHALMIC MINIATURE

On Cataract

I tell you that there are seven kinds of cataract, four of them curable and three incurable.

First of all let us talk about the curable varieties, and distinguish well-defined sorts from the doubtful.

The first of the curable cataracts looks like the purest white chalk. The second is bluish-white and is due to errors of diet causing excretions from the stomach. These are carried to the brain, thence to the eye, where they cause the disease. The third kind is also bluish-white and it is caused by severe headache, such as migraine, by excessive cold, too much worry, wailing and weeping, and similar troubles. The fourth variety of curable cataract is of a yellowish cast and arises from excessive drinking and eating, from the pain and complications of childbirth, and from the melancholic humor.

Benevenutus Grassus of Jerusalem,
De Oculis Eorumque Egritudinibus et Curis,
translated by Casey A. Wood, 1929.

NARROW-ANGLE GLAUCOMA

EFFECT OF MIOSIS ON THE NARROW-ANGLE MECHANISM AND INTRAOCULAR PRESSURE

OTTO BARKAN, M.D.

San Francisco, California

CASE HISTORY

The following case report illustrates the effect of the mechanical causal factors (size of the pupil, seclusion, and bombé of the iris) on closure and opening of the angle of the anterior chamber in narrow-angle glaucoma.

Mrs. A., aged 57 years, was first seen by her oculist in April, 1946. She gave a history of having suffered occasional pain and slightly blurred vision of the right eye three years previously. The tension was: R.E., 65 mm. Hg; L.E., 22 mm. Hg (Schiotz). A diagnosis of chronic glaucoma, right eye, was made. Pilocarpine was prescribed three times daily for the right and once daily for the left eye. The tension was reduced to: R.E., 32 mm. Hg; L.E., 22 mm. In August, 1946, the medication for the left eye was discontinued. Pressure in the right eye continued at this level until March, 1948, when it could no longer be controlled by miotics. Tension was then right eye 40 mm. Hg (three hours after the instillation of Carbachol); left eye 30 mm. Hg (without the use of miotics). Excavation of the optic disc with a corresponding field defect had developed in the right eye.

In April, 1948, the patient was seen by me in consultation. The eyes were pale and had never been congested. The corneal diameters measured 11.75 mm. in the horizontal meridian in each eye (normal = 11.5 mm.). The axial depth of the anterior chamber was 1.3 mm. in each eye by direct (uncorrected) readings from the Ulbrich drum, measured from the vertex of the cornea to the margin of a pupil 2.0 mm. in diameter. This is rather shallow, the average for the normal eye being 2.0 mm.

Diameter of the pupils was: R.E., 2.25 mm. (the last drop of Carbachol had been

instilled four hours previously); L.E., 1.75 mm. (no miotics had been used). The pupil of the left eye did not react to light or to convergence. It dilated to 2.25 mm. following instillation of 10-percent cocaine, indicating that the dilator was functioning and that there were no posterior adhesions. There was a small Krukenberg spindle in each eye.

The patient stated that the pupil of the left eye had always been small. History and physical examination were negative. No spinal puncture had ever been done.

Ophthalmoscopic examination showed excavation of the optic nervehead to the rim in the right eye and a normal optic disc with small physiologic excavation in the left eye. The visual field was contracted on the right eye and normal on the left.

Gonioscopic examination showed bombé of the iris and markedly narrow angles in both eyes. The opening to the angle was slightly narrower in the right eye and it was closed over a part of the upper circumference. There appeared to be little, if any, closure in the left eye. Iridectomy was advised.

On April 22, 1948, a peripheral iridectomy ab externo was performed on the right eye by her oculist. A fistulizing bleb developed which has normalized the pressure up to the present time. The pressure of the left eye has always been normal without the use of miotics.

At the time of the last examination on April 23, 1953, the pressure was: R.E., 18 mm. Hg; L.E., 32 mm. Hg (Schiotz), without miotics. The axial depth of the anterior chamber had deepened in the right eye from 1.3 mm. to 2.0 mm.; the left was unchanged at 1.3 mm.

Gonioscopy of the right eye showed the iris to be in a flat plane with some circular furrows. The bombé had collapsed. The angle

was widened in and adjacent to the area of the coloboma. It was only very slightly widened in other areas, evidently because adhesions had formed postoperatively—the result of an ab externo fistulizing incision which delayed reformation of the chamber and angle.

DISCUSSION

In a case of recently uncontrolled narrow-angle glaucoma in the noncongestive phase, there was difficulty in producing miosis of less than two mm. and of controlling the tension in the right eye. There was a spastic miosis of unknown etiology, perhaps congenital, in the left eye. The pupil was 1.75 mm. in diameter and was rigid. The tension of the left eye has generally been within normal limits without the use of miotics. The optic disc and visual fields were normal.

The axial depth of the anterior chamber was equal and unusually shallow in both eyes. However, the bombé was greater and the angle slightly narrower and partially closed in the right eye. The increased pressure in the right eye appeared to be the result of closure of the angle in part of the upper circumference. In both eyes the same predisposing factor, shallowness of the axial chamber depth, was present in measurably equal degree. This shows how critical the effect of the slightest change in size of the pupil can be in the presence of a predisposing iris bombé and narrowing of the angle.

The constant spastic miosis in the left eye which was greater than that which was ever achieved in the right eye by miotics had evidently kept the angle open sufficiently to pre-

vent closure of the angle, rise of pressure, and damage to the optic nerve.

CONCLUSION

A rise of pressure was prevented in the left eye by a spastic miosis of unknown etiology. In the right eye the miosis achieved by drops was never as great as that of the left eye without drops. The pressure in the right eye could not be controlled by miotics and operation was necessary. The course of events in the two eyes supports the view of the mechanical origin of increased pressure in primary narrow-angle glaucoma.^{1,2}

It might be maintained that the disturbance of innervation which caused the miosis in the left eye might also have caused a change in the secretion of the intraocular fluid or in the vascular supply of the ciliary body, thereby affecting the pressure of the eye. There is, however, no evidence to support this view and it would appear to be an unlikely explanation. On the other hand, there is a great deal of evidence to support the view that the size of the pupil was a critical mechanical causal factor in this case of narrow-angle glaucoma.²⁻⁴

Lagrange and Daltaer⁵ reported in 1926 that a tabetic miosis of long duration had had no influence on the course of "chronic glaucoma." However, it appears that they were dealing with chronic wide-angle (noniris-block) or "simple" glaucoma in which the size of the pupil in itself is known to have no demonstrable effect upon the intraocular pressure.^{1-3, 6}

490 Post Street (2).

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CONTAMINATION OF EYE MEDICATIONS: PRACTICAL METHODS OF PREVENTION

J. H. KING, JR., COL. (M.C.)*
Washington, D.C.

The role of contaminated eye medications as a cause of primary infections in the eyes of unsuspecting patients and in adding secondary infections to patients seeking eye treatment is well known. Although tragic results may ensue, the importance of such contaminations is not generally realized by many ophthalmologists. The medicolegal implications are only outweighed by consideration for the patient's vision.

The purpose of this paper is to offer several means of preventing contamination, some of which have not previously been reported in the literature.

INFECTION BY CONTAMINATION

The transference of infection from one patient's eyes to those of another, or to themselves, by the fingers of medical personnel is, of course, inexcusable. Physicians and nurses surely understand the need for hygienic measures and must recognize their responsibilities in allowing office aides, military corpsmen, and others to apply eye medications or to assist in examining procedures. This, as well as the possibility of unsterile instruments, such as tonometers, will not be dealt with in detail here.

An important means of transferring infection is by the use of contaminated solutions and ointments during eye examinations and treatments. A variety of organisms including pathogenic bacteria, viruses, and fungi have been found as contaminants.

MEANS OF CONTAMINATION

I. SOLUTIONS

A. DRUGGIST

Contamination of solutions may occur during commercial manufacture, as recently

proved in the case of sulfonamides and cortisone.⁴ Others have been traced to solutions dispensed by hospital pharmacies and retail druggists.

This may occur by preparing the original large stock solution in an unsterile manner or by contaminating the solution, stoppers, or bottle while transferring the solution to smaller bottles for dispensing. The use of proper preservatives may have been neglected.

Most eye medication solutions dispensed by pharmacies arrive from manufacturers in 15-cc. bottles with a top incorporating a dropper, or capped and accompanied by a dropper in the same package. Most of these droppers are grossly dirty and an occasional pretense at cleanliness is made by enclosing the dropper in a loose cellophane envelope.

B. PATIENT

The usual dropper-type bottle containing prescribed solutions is undoubtedly contaminated after a short period of use. This may do no harm if the medication is used by the same patient. We all know, however, that it is common practice for several members of a family to use a "good medicine" which soothes red eyes, or which has been left in the bathroom medicine cabinet for some time.

C. WARD, CLINIC, OR OFFICE PRACTICE

Contamination of eye solutions probably never occurs in a modern eye operating room which uses freshly made and sterilized medications under aseptic conditions. The most common place for solutions to become unsterile is on the ward dressing tray, in the clinic, or in a private office. The usual cause, and probably the sole offender, is the contaminated eye dropper which has touched an infected eye.

Such infection may be obvious, or the

* Chief, Ophthalmology Service, Walter Reed Army Hospital.

patient may be a "carrier" with the offending bacteria or virus in the conjunctival fluids, or a *Pseudomonas* may exist on the skin of the eyelids.

Less likely causes of contamination may occur, such as placing the dropper upon soiled gauze or touching the tip with the fingers. Contamination of the bottle top is also possible by leaving it open-face down on an unsterile surface while removing the solution.

Lowbury⁶ isolated *Pseudomonas aeruginosa* from hospital bottles containing "disinfectant" fluids used for sterilizing instruments, preparing the skin, and so forth. Contaminated solutions of one-percent Cetrimide (a quaternary ammonium compound) were from bottles closed by corks, and, in some instances, the load of contamination on the cork appeared to be heavier than that in the fluid.

Lowbury feels it is probable that contamination occurred through the handling of the bottles rather than by deposition from the air. No contamination was found after screw-cap bottles were used to replace stoppered ones, and the author quotes Nelson in stating that bacterial growth-promoting substances can be derived from cork.

The important fact is that *Pseudomonas aeruginosa* can survive in a disinfectant fluid such as a quaternary ammonium compound of high strength—a concentration many times higher than that employed in some eye solutions to maintain sterility and in solutions to sterilize eye instruments and tonometers.

Theodore¹ states that there is evidence that these compounds may be inactivated by some types of rubber, because of the curing agents used.

They are not advised by many authors for use against *Pseudomonas* and are not recommended in the New and Nonofficial Remedies published by the Council of Pharmacy and Chemistry of the American Medical Association.⁷ It is not probable, however, that freshly

made solutions discarded after one use will be contaminated.

Pseudomonas aeruginosa (*B. pyocyaneus*) is the most important and major offender in solutions. Theodore¹ cultured 26 bottles of fluorescein in use throughout a hospital and found that all of them were infected with *Pseudomonas aeruginosa*. Examination of 15 solutions in offices of ophthalmologists revealed 10 contaminated with this organism.

The same author quotes a report from another hospital where three *Pseudomonas* corneal ulcers were traced to contaminated solutions of eserine and saline which had been in use for only a short time and which had been prepared under sterile conditions.

Five of 18 ocular infections caused by *Pseudomonas aeruginosa* were traced by McCulloch² to eye solutions. He pointed out that the bacillus grows readily in fluorescein and eserine solutions but that the latter was most often found to be contaminated.

These reports are not unusual. Conversations with ophthalmologists reveal that *Pseudomonas* ocular infections are seen in many hospitals and it is apparent that few of these cases reach the literature.

An incident which must be embarrassing to every industrial ophthalmologist was recently reported.¹⁰ A state Health Department engineer and a bacteriologist investigated a "mysterious eye affection" which caused the loss of sight in several workers in a plant. *Pseudomonas aeruginosa* was found in an eye solution used in the medical department. *Pseudomonas aeruginosa* is frequently found on the normal skin, in sweat, and in feces. Under ordinary conditions it is only slightly pathogenic.

The bacillus is occasionally found in the flora of the normal eye. It may reach the eye from infection with *Pseudomonas aeruginosa* elsewhere, such as otitis externa and media, skin infections, infected burns, and so forth.²

It may cause no infection in an intact corneal epithelium. It is extremely virulent, however, in the abraded cornea such as that

following foreign body removal. The severe ulcer and purulent keratoconjunctivitis usually result in loss of the eye.³

Other than corneal involvement, the bacillus may cause conjunctivitis, meibomitis, endophthalmitis, and dacryocystitis.³ I have found it frequently in the discharge accompanying infected sockets in which integrated implants had been used. The organism can grow in practically any ophthalmic solution, including antibiotics.¹

The highly communicable epidemic keratoconjunctivitis has been spread by solutions accidentally contaminated with the virus in eye clinics and in physicians' offices.^{3,17}

II. OINTMENTS

Pathogenic bacteria may also contaminate ophthalmic ointments. It has been stated that, at present, there is no satisfactory method of manufacture which insures sterility.

Heat sterilization of the commonly used emulsions is not practicable and the addition of preservatives must be depended upon. Under sterile conditions, careful preparation of ointments by the large pharmaceutical manufacturers usually results in a sterile ointment.

Lehrfeld and Donnelly⁸ presented evidence that most new and unused tubes of ophthalmic ointments were sterile. (We have found no growth in 24 new tubes cultured.) They showed that once the tube was opened, the remaining contents were frequently contaminated with *Staphylococcus albus* hemolyticus, *Staphylococcus aureus* hemolyticus, fungi, and other organisms. We also have confirmed this in several instances.

These ointments contained commonly used eye medications, including sulfonamides and antibiotics. Theodore¹ feels that *Pseudomonas aeruginosa* may also contaminate ointments.

Again, as in solutions, eye ointments may be contaminated by the patient or the physician by touching an infected eye with the

tube while applying the medication. In attempting to apply ointment to a frightened child or a patient with marked inflammation or postoperative blepharospasm, it is often impossible to avoid touching the eye or lids.

The same ointment tube is frequently used for many patients in a hospital or clinic, and usually to the last drop. No one knows how many persons use the same tube in a household.

The fingers may contaminate the tube nozzle or the cap, and a broken tube may readily admit bacteria. Cork, sometimes used to plug the tube end, has been previously mentioned as favoring bacterial growth.

The mechanical action of small undissolved drug crystals in an ointment vehicle can cause corneal abrasions.⁹ This introduces a serious situation if the ointment is also contaminated and pathogenic bacteria are allowed free passage beyond the corneal epithelium.

PREVENTION OF CONTAMINATION

I. SOLUTIONS

A. Preparation of sterile solutions

Theodore^{1,4,10} has done much to bring about the assurance that pharmaceutical manufacturers must supply sterile eye solutions. The A.M.A. Council on Pharmacy and Chemistry requires sterility before council approval is given an ophthalmic solution, and the Food and Drug Administration now demands the same. Hospital and other pharmacies formulating and compounding eye medications are not controlled by these rigid requirements.

In order to insure sterility, it behooves each ophthalmologist to investigate the pharmacy making his solutions. The procedures recommended by Theodore¹ and by Hogan¹⁵ are excellent and will not be repeated here.

B. Maintenance of sterile solutions

As pointed out previously, the contamina-

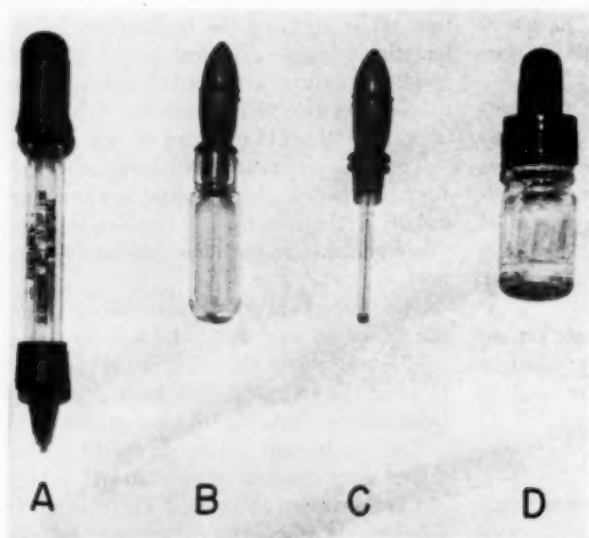


Fig. 1 (King). Types of sterile containers. (A) Disposable sterile container. (B) Small vial. (C) Small vial dropper. (D) Small screw-cap bottle with dropper.

tion of sterile eye solutions is in most instances due to used eye droppers being reinserted in the solution bottles. Other authors concerned with this problem are in agreement.^{1, 5, 11, 15, 17} Various methods are in use in different institutions in an effort to avoid this situation. Some will be mentioned here.

1. *Small sterile refillable containers.* One hospital uses a small vial* with a dropper (fig. 1-B and fig. 1-C). These are sterilized in an autoclave and filled with sterile solutions for use in the hospital operating room and clinic. Each vial holds from 0.3 to 0.5 cc. of collyria, enough for one application.

These vials are saved, disassembled, re-sterilized, and refilled. To avoid residual atropine, the rubber dropper bulb which has contained atropine is marked with a brass wire around the neck so that it again goes on a vial containing that same solution.

Although this procedure is expensive and tedious, it is a superior method of maintaining sterility; but it would be difficult to apply universally.

Figure 1-D shows a similar small screw-cap bottle† incorporating a dropper, with a volume of 1.0 cc. It may be used for several applications to the same patient after which it may be resterilized and refilled as has been described.

Its experimental use appears to preclude its general application in a large eye center because of its cost, waste, and the time consumed in preparation. One-use containers, however, could be employed to advantage in the operating room.

2. *Disposable sterile container.* As shown in Figure 1-A, this consists of a glass tube with a rubber bulb and a rubber tip.‡ It is filled with 0.5 to 1.0 cc. of various sterile, buffered ophthalmic solutions and is intended as a single dose disposable unit.

It may be used for several applications to the same eye. The rubber tip is immersed in alcohol and the rubber seal on the delivery tip snipped off by scissors when the medication is to be used. The scissors, or other in-

* "Dropul"—Courtesy N. Baker, apothecary-in-chief, The New York Hospital, 525 East 68th Street, New York 21.

† Pennsylvania Glass Products Co., Inc., Pittsburgh, Pa.—Courtesy Captain J. W. McNamara, Chief, Pharmacy Service, Walter Reed Army Hospital, Washington 12, D.C.

‡ "Steretainer"—Selney Company, Inc., 153 Waverly Place, New York 14.

strument used in cutting off the rubber end would, of course, also have to be sterile.

The advantages of this ingenious device are obvious, and it is certainly a commendable step forward. The disadvantages are the time consumed in sterilizing the tip and in maintaining sterile scissors.

It has been pointed out previously that *Pseudomonas aeruginosa* can grow in quaternary ammonium compound solutions used to sterilize instruments, indicating that, unless the solution is changed daily, some other method of sterilizing the scissors would appear advisable.

It is also possible to contaminate a stock disinfecting solution with atropine when a vial containing that solution is cut open with scissors which are then placed in the solution.

These disposable sterile containers are too expensive for use in a large clinic but are ideal for the eye operating room. The rubber components make their adoption by the military services questionable because of the long storage frequently involved. Although visible particles appeared in the solution when the bulb was squeezed, six containers were found sterile to culture.

3. *Sterile dried fluorescein.* Fluorescein solution is an excellent medium for *Pseudomonas aeruginosa* and is the one most commonly contaminated by the eye dropper. Efforts have been made to avoid the use of this stain in solution form and to apply it by other means.

Kimura¹² designed sterile fluorescein-impregnated filter paper strips which are touched to the conjunctiva in a dry form or after moistening with water or saline. A small compressed wafer of fluorescein which is placed in the conjunctival sac and dissolved by tears is manufactured commercially.* Both of these methods are excellent for the purpose intended.

4. *Disposable plastic eye dropper.* If the "dropper-bottle-top" applicator were elimi-

nated from office and clinic practice and replaced by separate sterile or clean eye droppers for one patient only, the problem of contamination of eye solutions would be negligible.

It was the practice in our clinic for some years to use individual glass eye droppers for each patient. Those used for atropine and similar solutions were kept separate. After one application the droppers were resterilized for further use.

Thygeson,¹³ several years ago, recommended that dropper-bottles be discarded and individual droppers be used to avoid the office spread of epidemic keratoconjunctivitis. Hogan and Nugent¹³ advise the use of multiple droppers.

Theodore¹ states that, when the dropper has touched an infected eye, if bacterial contamination is suspected, the dropper may be resterilized by boiling or by the use of alcohol; if viral infection is suspected, the dropper or the solution should be discarded. This procedure eliminates the possibility of dropper contamination of solution bottles, but it is time-consuming and expensive.

Droppers do not withstand many sterilizations. The safest technique would involve the use of bottles with screw caps flanged to overlap the neck and a dropper to be used only once. To discard a glass dropper after each application is obviously too costly.

In our clinic for the past six months we have employed a cheap disposable plastic dropper.† It consists of a one-piece plastic compressible tube, closed at one end. By pressing the closed end between the fingers, enough solution for one or two applications—four to five drops—can be drawn into the dropper. The tube is then thrown away and never touches another patient or the solution bottle again.

These droppers cost a fraction as much as the cheapest glass dropper and offer good insurance against contamination. Although they are not made of an inert material, as is

* "Tabloid," compressed fluorescein, Burroughs Wellcome & Co., Inc., New York.

† "Sanidrop," Marnel Company, Inc., 110 North St. Asaph Street, Alexandria, Virginia.



Fig. 2 (King). Use of disposable plastic eye dropper.

glass, they are not used for prolonged contact with solutions and no reaction has been noted between the dropper and the usual eye solutions.

They are packaged, "sanitized" by ultraviolet rays, but may be sterilized for operating room use by immersion in a fresh solution of benzalkonium chloride for 30 minutes.

Pathogenic bacteria have not been found on taking cultures from the unused droppers, and it is unlikely that airborne virus would infect them. We continue to use sterile glass droppers in the operating room and on the ward for postoperative local medication.

The disposability feature of these droppers offers other advantages in addition to eliminating dropper contamination of solutions. It is sometimes impossible to apply medications by a dropper without touching the conjunctiva of an inflamed blepharospastic eye. This may be *purposely* done using a disposable dropper.

Copious secretions should be removed by irrigation before applying any medication, as it is not effective in their presence. It is, of course, important not to allow the fingers to touch the eye.

In describing the application of eye solutions, most authors^{14,17} state that the upper lid should be raised at the same time the patient looks down, so that the solution may be dropped on the eye at the 12-o'clock position above the limbus and be allowed to

flow over the cornea. The solution is relatively undiluted and maximal absorption occurs through the cornea.

This technique may be used. However, there is a natural tendency for a person to look up rather than down when the eyes are opened, especially in the presence of photophobia.

It is difficult to look down with blepharospasm. In this case, the patient should be directed to look up and the dropper should then be touched to the lower cul-de-sac and the desired amount of medication deposited (fig. 2). The patient is then told to close his eyes and to look down immediately. The patient does not wince when approached from the side in this manner.

II. OINTMENTS

A. Preparation of sterile ointments

The collapsible tubes, commonly used to package ophthalmic ointments, are made of tin with a small amount of copper. These, and the plastic or metal caps, can be sterilized. The contents, however, usually contain a hydrocarbon base which breaks down upon heat sterilization; thus the addition of preservatives is necessary.

No ointment tube is labeled "sterile" and the Food and Drug Administration requires no more than 50 bacteria per gram of ointment.

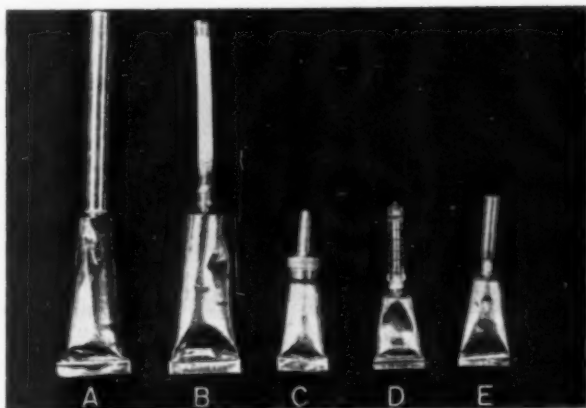
This is unsatisfactory, for, as Lehrfeld⁸ has stated, the mere fact that certain organisms are present is sufficient proof that pathogenic bacteria may also be present. The same author, however, showed that, in most instances, new unused tubes were not contaminated.

Recently, several large ophthalmic ointment manufacturers have changed their methods of production and every effort is being made to assure sterility.

B. Maintenance of sterile ointments

The average tube contains one-eighth ounce (0.60 gm.) of material. This allows

Fig. 3 (King). Disposable extension tubes and small ointment tubes. (A) Container with long cap. (B) Container with an extension of polyethylene tubing. (C) Container holding 1.7 gm. (D) Extension tube which may be broken off at the three-mm. markings. (E) Half-size container with polyethylene extension tube.



more than 20 generous applications of ointment.

If a tube is contaminated after several uses,* then the remaining applications will supply bacteria to an inflamed eye or an open wound. No doubt, the contamination increases the longer the tube is in use.

The major contamination of ointment tubes occurs, as in the case of eye droppers, from touching the tip to the patient's infected eye. Some contamination is possible from fingers, but an airborne origin is doubtful.

In our operating room, all tubes are new and are sterilized externally by being placed in a solution of fresh benzalkonium chloride for one hour. After one application, these tubes are returned to the clinic for further use. Only new tubes are employed on the wards in recent postoperative cases, and they, too, are returned to the clinic after one use. Any tube which has accidentally touched an eye is discarded.

1. *Disposable extension tubes.* As with a dropper, the medication from an ointment tube may be best applied to a blepharospastic eye, in many instances, only by touching it with the tip. With this in mind, we have used a container with an extension of polyethylene tubing for postoperative treatments (fig. 3-B).

After application, about three mm. of the tubing were cut off by scissors carried on

the tray in a disinfecting solution. Separate scissors were used for atropine. A long cap was immediately screwed back upon the container (fig. 3-A). In this way many applications of "sterile" medication could be obtained from the same tube.

The effort involved in this procedure has not made its use popular in the clinic.

A similar extension tube of foil or plastic, serrated or weakened at about three-mm. intervals, can be made so that it can be broken off at these markings (fig. 3-D). A small amount of ointment should always be expressed from the tube, but not used, before each use.

2. *Small tubes.* The ideal eye ointment should be packaged in small individual sterile tubes which can be disposed of after one application. The expense of manufacture, however, prohibits this.

A slightly larger container (fig. 3-C), holding about one sixteenth ounce (1.7 gm.), has been requested from the manufacturer as an alternative. It may also have an extension tube which is cut or broken off, as previously described, if desired. This insures relative sterility for surgical and clinical patients and precludes keeping a container for a long period of time.

Again, it must be stressed that a new tube should be employed in all eye wounds. Reinfection, from larger tubes which have become contaminated, may account for many



Fig. 4 (King). Disposable sterile applicator.

failures in treatment, such as those which occur in mass treatment programs for trachoma. An additional advantage in using small tubes for home therapy is the lessened waste of medication.

3. *Disposable sterile rods.* The use of a glass rod without proper sterilization for applying an eye medication to a number of patients is malpractice. Individual sterile paper rods, to be disposed of after one use, are convenient and safe.

A small amount of ointment is squeezed from the tube onto the end of the applicator (fig. 4). It is then applied to the lower cul-de-sac and the rod thrown away (fig. 5). The flattened end of the disposable eye dropper previously mentioned may be similarly used as an ointment applicator. Sterility of the tube is thus maintained.

4. *Plastic containers.* Small plastic tubes to be used for several applications of oint-



Fig. 5 (King). Application by sterile paper rod to lower cul-de-sac.

ment or solution for individual patients would be desirable because of their low cost, but this is not possible at present.

Even the most inert plastics, such as polyethylene and vinyl, are not usable with any degree of certainty. After variable periods of time, a process of "breathing" occurs in which oxygen enters and affects certain medications.

Most solutions or ointments packaged in plastic containers also suffer from "bleeding," which, in time, changes the strength and composition by diffusion through the plastic wall. Medicants containing acids cannot be packaged in plastic for one or both of these reasons.

Sterility under such circumstances would also be open to question, especially after storage and delayed use.

Further investigations are in order to develop an ointment vehicle which can be sterilized with the medication and marketed in small tin containers labeled "sterile." The Armed Forces Procurement Agency requires sterility in ointments as well as solutions.

Many bases used in commercial ointments contain stiff petrolatum which is immediately squeezed out of the conjunctival sac onto the lids. The ideal base should have a soft consistency and be inert and nonirritating. The medicament should be homogeneously dispersed in the base and milled so that the crystalline particles are less than 10 microns in their largest dimension. A "gritty" eye ointment is dangerous.

RECOMMENDATIONS

I. OPHTHALMIC SOLUTIONS

- A. Demand sterility from the manufacturer or dispensing pharmacist.
- B. Discard dropper-top bottles for clinic and office practice and use screw caps only. These should have tapered tops to prevent contamination in handling and the tops should be replaced as soon as the solution is withdrawn.

- C. Bottles should hold no more than 15 cc. and preferably less. They should be replaced at least bimonthly.
- D. Disposable plastic droppers, for one use only, are ideal for clinic and office use.

II. OPHTHALMIC OINTMENTS

- A. Demand sterility from the manufacturer.
- B. Use new containers for all wounds, traumatic or postoperative, if ointment is desired.
- C. Use sterile disposable paper rods for individual applications in the office, clinic, and on the wards.
- D. Use small "half-size" tubes for home therapy.
- E. Express a small amount of ointment before each use.

SUMMARY

The frequency of contamination of solutions and ointments for use in eye examinations and medications is well known. Pseu-

domonas aeruginosa (*B. pyocyaneus*) is the most common and most dangerous contaminant of solutions.

Several methods of maintaining sterility are discussed. For solutions, the most practical and economical means in clinic and office practice is the use of small screw-cap bottles and disposable plastic eye droppers, discarded after each use. In the case of ointments, small containers holding about one-sixteenth ounce, which allow several applications of sterile medication, are advised, especially for self-medication. In the clinic, sterile disposable rods may be used to apply ointment to the lower cul-de-sac.

The sterility of eye medications of commercial manufacture is the responsibility of the Food and Drug Administration. Sterility in hospital and dispensing pharmacies is the charge of ophthalmologists using those facilities. It behooves every eye physician to be vigilant in maintaining sterility in clinic and office practice.

Walter Reed Army Hospital (12).

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PIGMENTARY GLAUCOMA AND ITS RELATION TO KRUKENBERG'S SPINDLES*

F. PHINIZY CALHOUN, JR., M.D.
Atlanta, Georgia

In 1951 Sugar¹ reported three cases of a form of glaucoma which he designated as "pigmentary glaucoma." Two of these he had described in detail in 1949.² The clinical picture was exactly alike in the three cases.

First, the condition occurred in young individuals. Secondly, there was a marked dispersion of pigment granules in the anterior chamber evidenced by the presence of Krukenberg's spindles on the posterior corneal surface and the deposition of pigment granules in the trabecular spaces. Thirdly, all cases responded to the mydriasis provocative test by a paradoxical increase in intraocular pressure, yet there was no narrowing of the chamber angle. Two cases were in myopes and the third was in a moderate hyperope.

The pigment deposition in these cases was so marked that it suggested itself as the possible cause of the increased intraocular pressure. Sugar believed the condition to be a clinical entity and a form of secondary glaucoma.

Realizing the extreme difficulty of assessing directly the role of pigment in the production of glaucoma in such cases, I have attempted an indirect approach to the problem by clinical analysis of cases of Krukenberg's spindles with glaucoma and cases of Krukenberg's spindles without glaucoma. This report then deals with the study of six patients whose clinical picture represents to me modifications of the condition "pigmentary glaucoma," and the study by means of simple clinical tests of a group of five patients with Krukenberg's spindles and no glaucoma.

*From the Department of Ophthalmology, Emory University School of Medicine, and the Grady Clay Memorial Eye Clinic, Grady Memorial Hospital. Presented at the 88th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, June, 1952.

Since the Krukenberg's spindle is the common denominator of all the cases under consideration and is the chief indicator of the general pigmentary disturbance in the eye, let me define the term as used in this discussion.

All cases had in one or both eyes a narrow or rounded oval of rusty brown pigment two to six mm. long and 0.5 to three mm. wide situated in a vertical or slightly oblique line on the posterior surface of the cornea. The larger spindles were usually quite obvious with oblique illumination and loupe, or visible in the ophthalmoscopic reflex, but lesser degrees of spindle formation were visible only with the biomicroscopy. As pointed out by Goar in 1928,³ the corneal microscope in cases of Krukenberg's spindles reveals that the pigmentation is considerably more diffuse than one would suspect from the examination with the naked eye or loupe.

There was considerable variation in size, shape, and intensity of the spindle in different patients. In two of the patients with glaucoma the spindle was unilateral and the pigment in the other eye was not sufficiently dense to form a spindle. All cases showed varying degrees of atrophy of the pigment seam of the iris, and pigment deposition in the trabecular meshwork, anterior surface of the iris, and equatorial region of the lens.

In 1941, Evans, Odom, and Wenaas⁴ analyzed 202 cases of Krukenberg's spindles, 107 of them from the literature, and 95 unpublished cases gathered by questionnaire. These authors found that approximately 75 percent of the cases were bilateral and approximately 70 percent occurred in myopic patients. Of interest to the present study was the fact, reported by these authors, that of their group as a whole 62 percent occurred in females, whereas of the patients under 30

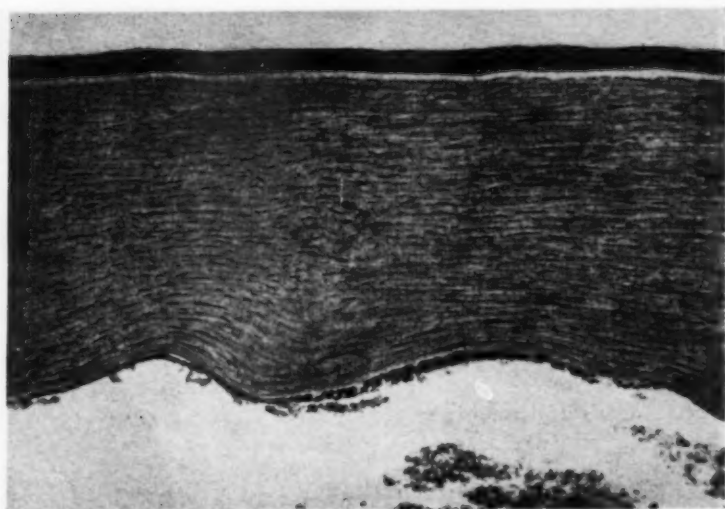


Fig. 1 (Calhoun). Microscopic appearance in a case of Krukenberg's spindle, showing pigment in the endothelial cells on the posterior surface of the cornea. (From Hanssen.²)

years of age, the ratio was reversed and 68 percent occurred in males.

Only three cases of Krukenberg's spindles have ever been examined histologically. The first by Hanssen in 1923² showed a degeneration of the retinal layers of the iris pigment and to a less extent of the ciliary body. The endothelial cells on the posterior corneal surface were orderly and regular but were filled with pigment (fig. 1). Free pigment was seen to infiltrate the trabeculum and Schlemm's canal and at the peripheral cornea anterior to Descemet's membrane. Fine pigment dust was seen on the iris surface and on the lens capsule. The pigment seam of the iris was degenerated and there were dehiscences in the posterior epithelium of the iris. Bleached sections showed degeneration of the epithelial cells (fig. 2).

Neither the case of Kayser^{6,7} nor that of Korobova,⁸ both reported in 1929, had published illustrations but both authors stated that their cases revealed exactly the same changes as the case of Hanssen.

Of the 202 cases of Krukenberg's spindle analyzed by Evans, Odom, and Wenaas, 25 cases had the presence or history of inflam-

mation of the eye, 12 had cataract, and 12 had glaucoma. The reported incidence of glaucoma was therefore low.

Duke-Elder⁹ feels that a Krukenberg's spindle represents the accentuation of a very general atrophic process in which the pigment derived from the uveal tract is deposited on the corneal endothelium and aggregated into the space of an approximately vertical spindle. The theory that the condition is congenital and associated with persistent pupillary membrane has largely been disproved.

In this analysis of six cases of glaucoma associated with Krukenberg's spindles, several interesting results were obtained:

1. All cases were in white males between the ages of 23 and 37 years at the time of onset of the glaucoma. The average age of the group was 31.7 years.

2. All cases were myopic. The iris color was brown in five patients and blue-gray in one.

3. Krukenberg's spindles were present in all patients at the time of the first discovery of glaucoma.

4. Gonioscopically, all cases had deep an-

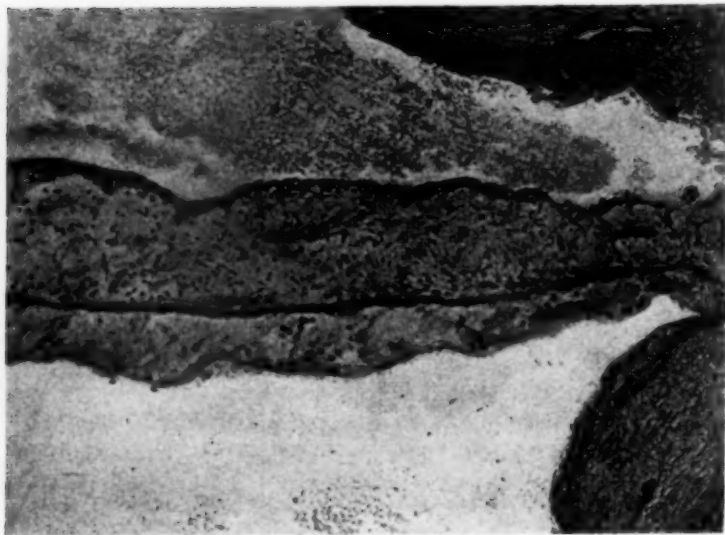


Fig. 2 (Calhoun). Microscopic appearance of a bleached section from the same case as shown in Figure 1, showing degeneration of the epithelial cells on the posterior surface of the iris. (From Hanssen.²)

terior chambers and open angles. No trabecular synechias were seen except in several instances immediately adjacent to an operative site. All cases showed a dense ring of pigment involving chiefly the posterior portion of the trabecular meshwork, but this degree of pigmentation could not be said with certainty to be greater than is sometimes seen in many normal brunet eyes. The diagnosis of glaucoma could not be made from the gonioscopic appearance alone.

5. In comparing the clinical course of the six cases there seemed to be an inverse relation between the severity of the glaucoma and the size of the Krukenberg's spindles in that the two patients with the largest spindles (Cases 1 and 4) appeared to be the easiest to control. This may have been due to the fact that one (Case 1) was a low-tension glaucoma and the other had early operation in both eyes.

In the four cases in which there was a definite individual difference in the size of the spindle between the two eyes, however, the largest and most dense spindle occurred in the eye with the most advanced glaucoma-

tous change. In two of these cases the most involved eye was also the most myopic. In one case the spindle lessened two years after operative control. In all others, the spindles have remained unchanged whether tension was controlled or not.

6. Operations had been performed on four of the six patients. Ten of the 13 operations performed were on two patients who had five each. Ten of the operations were trephinations. In one patient a previous complete iridectomy on each eye had been unsuccessful. A Herbert's trap-door sclerotomy was successful in one case. The cases with multiple operations frequently had severe post-operative hemorrhages.

7. In a few of the patients conditions were suitable for provocative tests. The water-drinking test was performed in three cases with positive results in Cases 1 and 2, but negative results in Case 3. The mydriasis test in Cases 2, 3, and 6 was negative but in Case 1, which showed great pigment disturbance, the result was positive.

8. The physical characteristics of this group of patients were unusual. The average

height was six feet one inch, and the average weight was 198 pounds. Despite the presence of a mild thyroid deficiency and mild hypertension in Case 1, suggestive sterility in Cases 4 and 6 and gigantism in Case 2, no definite endocrine disorder common to the group could be demonstrated. It was felt, therefore, that an underlying endocrine imbalance was only an extremely presumptive association in this small group of cases.

As a comparison to the group of patients just described, tests of the aqueous outflow mechanism were performed on five patients who had Krukenberg's spindles but no signs or symptoms of glaucoma. Accordingly, these patients were given a provocative water-drinking test and mydriasis test, and the facility of aqueous outflow was measured by tonography as performed with the electronic tonometer. All positive tests were repeated and confirmed.

The water-drinking provocative test was strongly positive in both eyes of two patients (Cases A and D) and was slightly positive in one eye of another patient with diabetes, monocular detachment of the retina, and cataract (Case C).

The mydriasis test failed to produce a change in intraocular pressure in any case. During mydriasis no free-floating pigment particles could be seen in the anterior chamber in any case.

Tonography was not performed in one of the patients with a positive water test (Case D), but the facility of aqueous outflow was normal in all other cases.

Gonioscopically, all cases showed a deep anterior chamber, a wide and open angle, and varying degrees of pigmentation of the trabeculum.

DISCUSSION

It is impossible to prove whether a dispersion of pigment granules in the meshwork of the trabeculum can alone be the cause of an increased intraocular pressure. It is well recognized that in some cases of uveitis and in cases of exfoliation of the lens capsule

the trabeculum is loaded with pigment and debris yet the tension is normal.

The positive response to the water test in the cases of simple Krukenberg's spindles actually tells us nothing definite concerning pigment in the trabeculum, but only that there is an impairment at some point in the outflow mechanism. This assumes of course that hypersecretion is not a factor.

I believe that the pigment is only an indication of some concomitant degenerative disease in the eye. That glaucoma is more likely to develop in such eyes is an indication of the unhealthy state of the eye dependent on factors other than a simple mechanical blocking of the trabecular meshwork.

The paradoxical elevation of tension following mydriasis in the cases of glaucoma associated with Krukenberg's spindles reported by Sugar, and present in one of my cases, has yet to receive an explanation. Since the chamber angle is not narrowed in such cases the most likely explanation would be a reduction in the absorptive surface of the highly pigmented iris when it is fully dilated.

CONCLUSIONS

1. The Krukenberg type of corneal pigmentation is probably more common than is generally believed.

2. Six cases of chronic, simple wide-angle glaucoma with varying degrees of Krukenberg's spindles are reported. This association occurs predominantly in young myopic males of large stature. The clinical manifestations and course of the glaucoma in these cases was no different from that occurring in the same age group without Krukenberg's spindles, except that in one case the mydriasis provocative test produced a paradoxical elevation in intraocular pressure, a characteristic described by Sugar.

3. In five patients with Krukenberg's spindles but no glaucoma, the mydriasis provocative test failed to produce a rise in intraocular pressure and no free particles of pigment could be seen in the anterior chamber during the test. The measurement of the

facility of aqueous outflow was normal in all cases. In two of the cases, however, the water-drinking provocative test was strongly positive, indicating a glaucomatous tendency.

4. I believe that corneal pigmentation of the Krukenberg type is an expression of a concomitant degenerative condition of the eye in which glaucoma is likely to supervene, but I found no definite evidence that the pigment deposition alone was producing the glaucoma.

5. As a point of practical value, I have produced evidence that the water-drinking provocative test performed in young myopic males who have corneal pigmentation of the Krukenberg type will occasionally lead to the early diagnosis of simple glaucoma.

GLAUCOMA ASSOCIATED WITH KRUKENBURG'S SPINDLES

CASE 1

I am indebted to Dr. William J. G. Davis of Washington, D.C., who has kindly furnished the early records of this case.

The patient was first discovered to have myopia in 1935 at the age of 26. In 1937, the vision of the right eye was 20/15 with $-3.25D$. sph., and vision

of the left eye was 20/15 with $-4.75D$. sph. $\ominus -0.25D$. cyl. ax. 90° . In 1943 the vision of the right eye was 20/15 with $-4.00D$. sph. and of the left eye 20/15 with $-6.0D$. sph.

In 1944 and 1945, examinations by an oculist in another city found the vision of the right eye correctible only to 20/30, and the left to 20/15, but no cause for this was determined. In November, 1947, corrected vision right eye was 20/40 with $-4.5D$. sph. $\ominus -0.5D$. cyl. ax. 180° , and vision left eye was 20/15 with $-6.0D$. sph. $\ominus -0.75D$. cyl. ax. 60° .

Tactile tension was normal. Following the instillation of homatropine hydrobromide (two-percent solution) and *paredrine* hydrobromide (one-percent solution), the intraocular pressure rose to 56 mm. Hg (Schiotz) right eye, and 26 mm. Hg (Schiotz) left eye. There was no pain or congestion accompanying the elevated tension. Following the use of miotics the tension dropped promptly to 18 mm. Hg in each eye.

When first examined by me on March 2, 1948, his corrected vision was 20/30 in the right eye and 20/20 in the left eye. Both anterior chambers were very deep. Iris color was a medium dark brown.

There was marked evidence of pigmentary disturbance especially in the right eye. The surface of the iris showed numerous granules and flecks of brown pigment. There was a large roughly triangular area of pigmentation on the posterior corneal surface of the right eye, which was seen as a narrow vertical spindle in diffuse light. A small collection of fine pigment dots was seen on the posterior corneal surface of the left eye but the

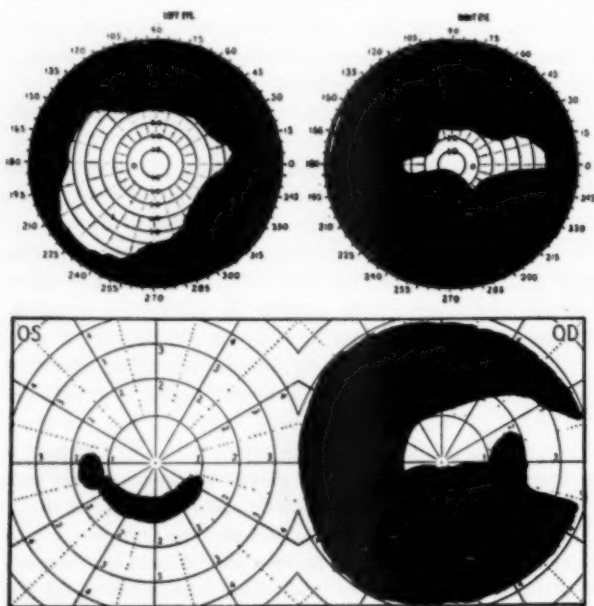


Fig. 3 (Calhoun). Case 1. Visual fields on November 20, 1947. Perimetric field with a 2/330 mm. test object; tangent screen with a 2/2,000 mm. test object.

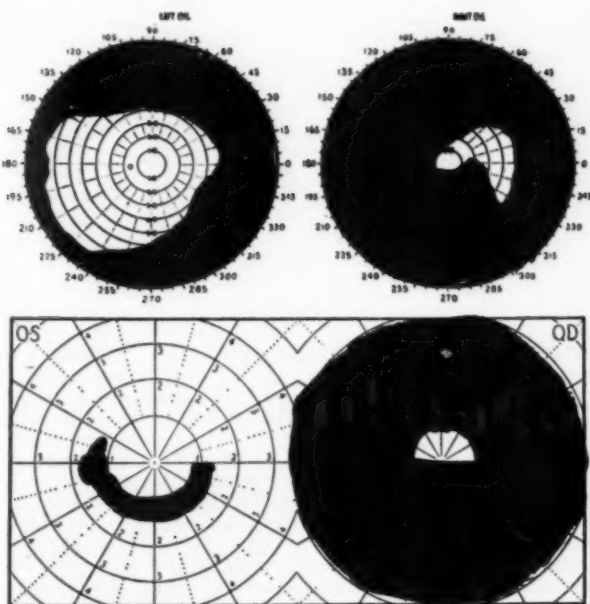


Fig. 4 (Calhoun). *Case 1.* Visual fields on November 1, 1951. Perimetric field with a 2/330 mm. test object; tangent screen with a 2/2,000 mm. test object.

collection was too small to form a spindle. No pigment deposits were seen on the lens.

Gonioscopy revealed an open angle and a dense ring of pigment in the trabeculum. This pigmentation was most marked inferiorly in the right eye. There were no trabecular synechias. Intraocular pressure was 18 mm. Hg (Schiotz) right eye, and 15 mm. Hg (Schiotz) left eye. The right optic disc showed marked glaucomatous cupping and atrophy and the left disc moderate glaucomatous cupping. Visual fields (fig. 3) showed marked changes.

The patient has been seen at frequent intervals and the tension has been easily maintained below 20 mm. Hg (Schiotz) by the use of miotics. When last seen on March 2, 1952, refraction revealed the vision of the right eye to be 20/30 with $-5.0D$. sph. $\ominus -0.5D$. cyl. ax. 180° , and of the left eye to be 20/15 with $-7.0D$. sph. $\ominus -0.75D$. cyl. ax. 90° . The extent and intensity of the pigmentary deposition have remained unchanged since the first examination. Visual fields at this time were as shown in Figure 4.

On October 6, 1951, on a fasting stomach, a water provocative test was performed. The intraocular pressure rose in 45 minutes from a pretest level of 17 mm. Hg in the right eye to 25.4 mm. Hg, and in the left eye from 12 mm. to 20 mm. Hg, thereafter gradually returning to normal.

On March 1, 1952, after the patient had had no medication for 20 hours, tonography revealed a normal facility of outflow of aqueous in each eye. In the right eye of the tension changed from 18.8 mm. Hg to 13.8 mm. Hg in four minutes to give a "C" factor of 0.10–0.15, and in the left eye from

15.6 mm. Hg to 9.4 mm. Hg to give a "C" factor of 0.20.

A mydriasis test performed later gave poor pupillary dilatation and no change in intraocular pressure.

The patient's average weight was 173 pounds and his height was six feet, one and one half inches. The patient had never been very robust but was in good general health. Sexual function was said to be normal. A complete physical examination in 1949 revealed short tapering fingers, normal hair distribution, and no prognathism. Initial blood pressure was 150/94 mm. Hg, and on subsequent examinations it ranged from 135/82 to 142/90 mm. Hg.

Routine laboratory procedures were normal except for albuminuria which had been present for 20 years. Kidney function tests were normal. Basal metabolic rates were minus-six percent and later minus-11 percent.

Fluoroscopy of the heart and lungs revealed only calcified hilar nodes. X-ray examination of the skull revealed a small normal sella turcica. A small area of parasellar calcification was thought to be in the right petroclinoid ligament and not in the internal carotid artery.

CASE 2

A 29-year-old white man who complained of failing vision in the left eye was found to have glaucoma in both eyes. Myopia had been discovered at the age of 22 years and had been progressive.

Examination on January 9, 1946, showed vision of right eye to be 20/15 with $-2.0D$. sph. $\ominus -2.0D$.

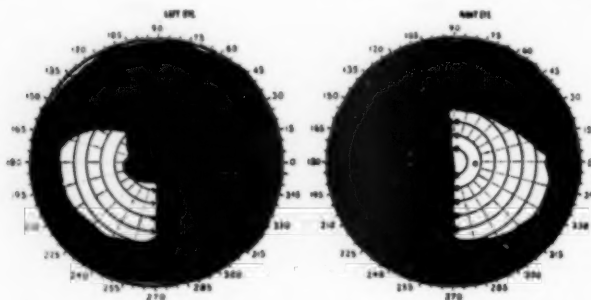


Fig. 5 (Calhoun). Case 2. Perimetric field taken on January 9, 1946, with a 2/330 mm. test object.

cyl. ax. 105°, and of left eye 20/100 with -4.5D. sph.

The anterior chambers were deep. The pupils measured four mm. in diameter. The irises were light brown in color.

There was a vertical spindle of pigment on the posterior surface of the right cornea. The collection of pigment in the left eye was not sufficient to form a spindle. The right eye showed a few early posterior cortical lens changes.

There was early glaucomatous cupping in the right optic nerve and marked glaucomatous cupping in the left optic nerve. Intraocular pressure was: R.E., 48 mm. Hg, and L.E., 44 mm. Hg (Schiotz). Visual fields showed marked defects in both eyes (fig. 5).

A complete iridectomy performed elsewhere on each eye did not result in permanent subconjunctival filtration and the tension returned to the preopera-

tive level. A trephination with peripheral iridectomy was performed in the right eye on May 21, 1946, and in the left eye on December 3, 1946. The post-operative course was prolonged in the left eye due to recurrent anterior-chamber hemorrhages, but good subconjunctival filtration resulted and the tension has remained between 14 and 20 mm. Hg (Schiotz) since that time.

The tension of the right eye remained below 30 mm. Hg until June, 1949, when it began to show constant elevation, on occasions reaching 50 mm. Hg despite a variety of miotics. On November 22, 1949, a trephination with peripheral iridectomy was performed on the right eye. Subconjunctival filtration soon ceased and the intraocular pressure has remained almost consistently between 30 and 35 mm. Hg since that time. There has also been further loss in visual field (fig. 6), central vision, and an increase in myopia.

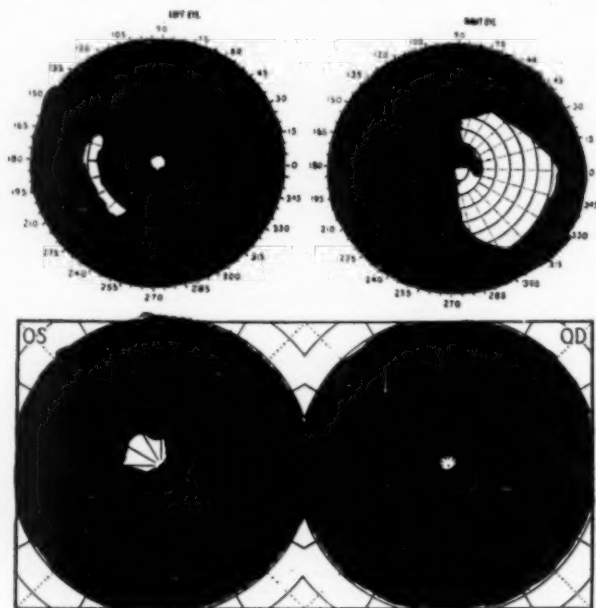


Fig. 6 (Calhoun). Case 2. Visual fields on April 30, 1952. Perimetric field taken with a 2/330 mm. test object; central field with a 2/1,000 mm. test object.

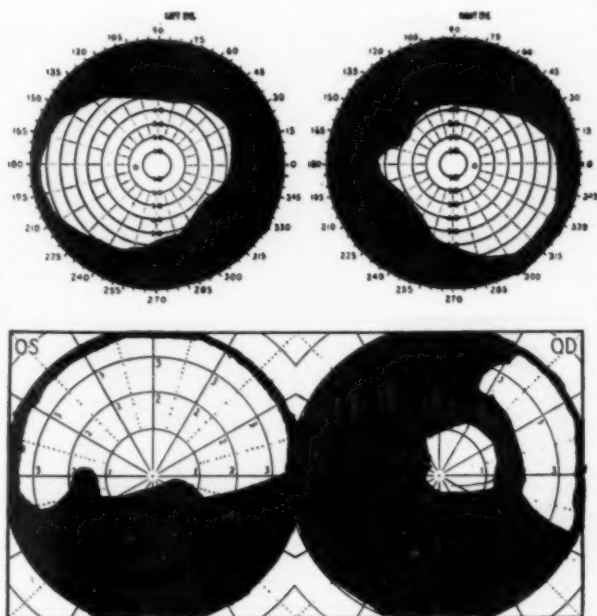


Fig. 7 (Calhoun). Case 3. Visual fields on March 31, 1949. Perimetric field taken with a 2/330 mm. test object; central field with a 3/1,000 mm. test object.

On April 30, 1952, refraction revealed: R.E., $-5.5D.$ sph. $\ominus -0.5D.$ cyl. ax. 90° to give 20/30; and L.E. $-5.0D.$ sph. to give 20/400.

On this date, slitlamp examination revealed the pigment changes on the posterior corneal surface to be as described in 1946. There was marked deposition of pigment flecks on the surface of the iris especially in the right eye. There was no atrophy of the pigment seam of the iris. There was mild iridodonesis in both eyes; this had been first noted in October, 1950. Pigment deposits were seen inferiorly in each lens just posterior to the equator.

Gonioscopy in the right eye revealed a wide angle and a narrow dense ring of brown-black pigment in the trabeculum. The inner aspect of the trephine opening appeared closed and no iris was incarcerated at the site of the iridectomy. No trabecular synchias were seen. In the left eye the equator of the lens appeared to be pinched into the trephine opening which was filtering subconjunctivally. There was no iris incarceration at the site of the iridectomy and no trabecular synchias, but the pigment ring was much less evident than in the right eye and inferiorly was almost absent.

The patient, like his father, was six feet six inches tall and weighed 240 pounds. He was in good general health. There were no signs or symptoms of endocrine disturbance and his blood pressure was normal. X-ray examination of the skull revealed small areas of calcification in the diaphragm sellae and in the petroclinoid ligaments. No calcification in the pituitary gland or walls of the internal carotid arteries was noted.

CASE 3

A 43-year-old man, who was first seen by me in March, 1949, had been treated for glaucoma since its accidental discovery in 1938. Myopia had first appeared in about 1936, when the patient was aged 29 years, and had remained essentially stationary.

Examination revealed the vision to be 20/15 in each eye with a $-2.0D.$ sph. $\ominus -0.5D.$ cyl. ax. 90° in the right eye and a $-2.25D.$ sph. $\ominus -0.75D.$ cyl. ax. 15° in the left eye. The horizontal diameter of the cornea was 12 mm. in each eye.

Biomicroscopy revealed deep anterior chambers. In each eye there was a wide triangular area of fine posterior corneal pigmentation which was concentrated centrally in the form of a narrow spindle when first seen in diffuse illumination, and of equal size in the two eyes. There was no atrophy of the pigment seam of the iris and no pigmentary deposits on the lens. The surface of the iris contained fine scattered dots and flecks of brown pigment. The lens was clear.

The discs were small and showed glaucomatous cupping and atrophy, more marked in the right eye. The visual fields showed marked defects (fig. 7). Intraocular pressure was 38 mm. Hg (Schiotz) in the right eye and 36 mm. Hg in the left eye.

Gonioscopy revealed the angle to be open all around in both eyes. Superiorly the trabeculum contained practically no pigment but inferiorly in both eyes there was a narrow, rather dense band of pigment in the posterior portion of the trabeculum.

Despite trial with a variety of miotic drugs, the intraocular pressure remained elevated and on

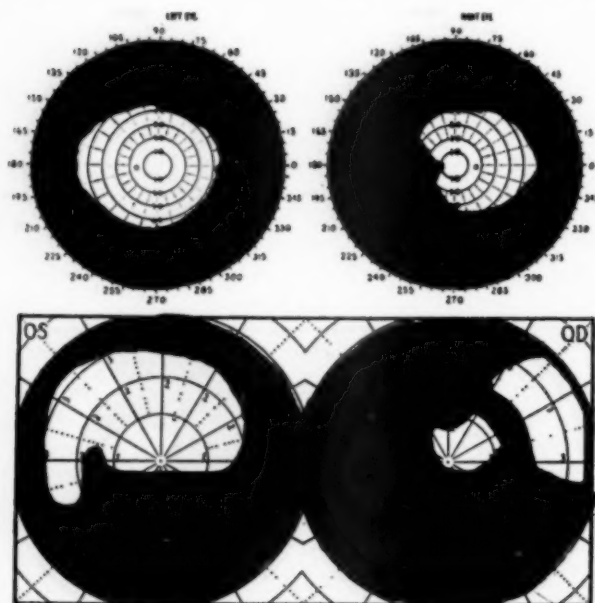


Fig. 8 (Calhoun). Case 3. Visual fields on March 23, 1952. Perimetric field taken with a 2/330 mm. test object; central field with a 3/1,000 mm. test object.

April 8, 1949, a modified Herbert trap-door sclerotomy was performed on the right eye. At operation, it was felt that the anterior chamber contained fluid vitreous. Postoperatively, the tension in the right eye was more readily controlled than before operation, although the use of miotic drugs was still necessary.

Periodic examinations since that time have shown the tension of the left eye to be fairly well controlled. When the patient was last seen on March 23, 1952, his corrected vision was 20/25, right, and 20/15, left. There was no subconjunctival filtration over the site of the previous operation on the right eye.

Biomicroscopy revealed that the degree of posterior corneal pigmentation was less than when first seen in 1949, and the pigment spindles were only faintly visible. Gonioscopy now revealed a few scattered trabecular synechias in both eyes. In the right eye the iris was adherent to the cornea at the operative site. Visual fields (fig. 8) showed further loss in both eyes. Intraocular pressure was 20.4 mm. Hg (Schiotz) right eye and 19.1 mm. Hg left eye.

After the omission of all medication for 56 hours, intraocular pressure was found to be 46 mm. Hg (Schiotz), right eye, and 40 mm. Hg, left eye. After repeated instillations of homatropine hydrobromide (two-percent solution) and neosynephrine hydrochloride (10-percent solution) the pupil dilated to six mm. in each eye but the tension remained essentially unchanged during the hour following the dilatation. No free pigment could be detected in the anterior chamber during dilatation.

A water provocative test performed only 17 hours after the patient had received one instillation of

eserine salicylate (0.25-percent solution) failed to demonstrate any increase in intraocular pressure during the hour following the test.

The patient was in good general health. He weighed 173 pounds and was six feet one-half inch in height. Several general physical examinations revealed no symptoms or signs of any endocrine disorder. His blood pressure was 150/90 mm. Hg. The usual laboratory examinations were normal.

CASE 4

A 37-year-old man was first seen on March 3, 1949, complaining of blurred vision in the left eye of several months' duration. He had worn glasses for near-sightedness for 15 years. Refraction revealed: -3.5D. sph. \ominus -0.5D. cyl. ax. 90° in the right eye to give 20/30; and -4.0D. sph. in the left eye to give 20/40 vision.

The iris color was light brown, and examination with oblique illumination and loupe revealed a dense vertical pigment spindle on the posterior corneal surface (fig. 9). The anterior chambers were deep and corneal biomicroscopy revealed that the very fine pigmentation on the posterior surface of the cornea covered a wide area (fig. 10). In the ophthalmoscopic reflex the spindle was small, narrow, and much less evident, and detectable only in the left eye (fig. 11).

Numerous small dots and flecks of brown pigment were scattered on the iris surface of both eyes, and, following a later dilatation of the pupils, a line of pigment could be seen on the inferior surface of the lens in the left eye just posterior to the equator. The right eye showed considerable atrophy of the pigment seam of the iris inferiorly; the left

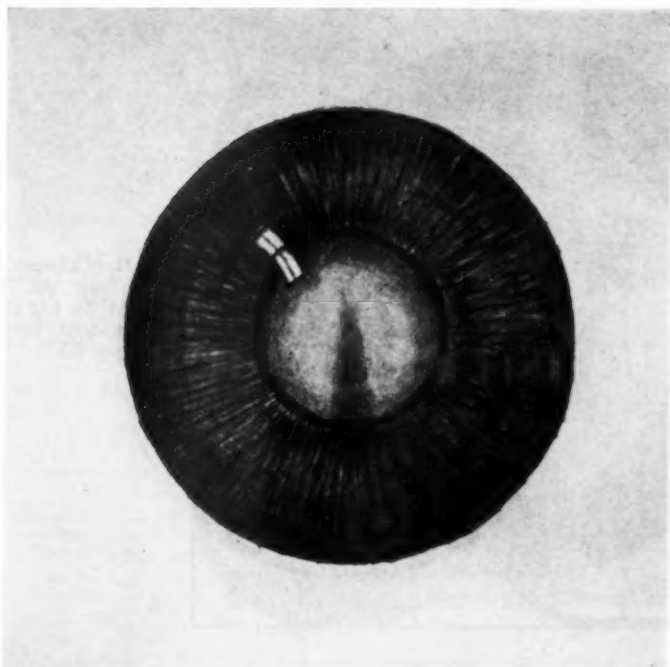


Fig. 9 (Calhoun). *Case 4.* Appearance of the position and size of the Krukenberg's spindle in the left eye as seen with oblique illumination and loupes.

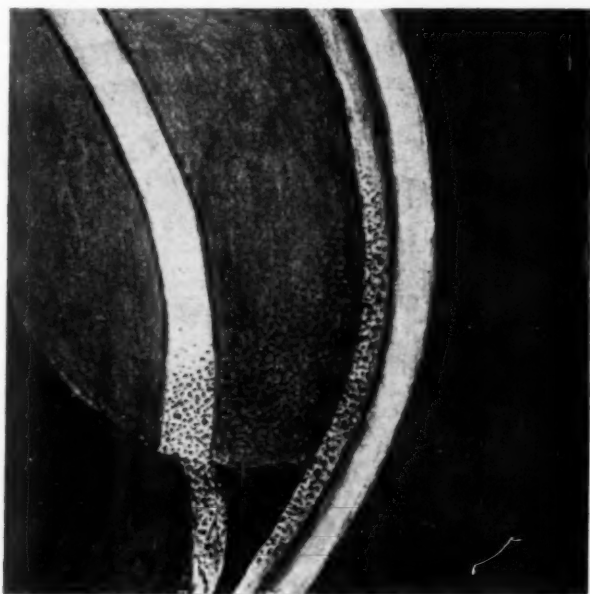


Fig. 10 (Calhoun). *Case 4.* Bi-microscopic appearance of left cornea to show that the pigmentation on the posterior corneal surface extends over a wide area.

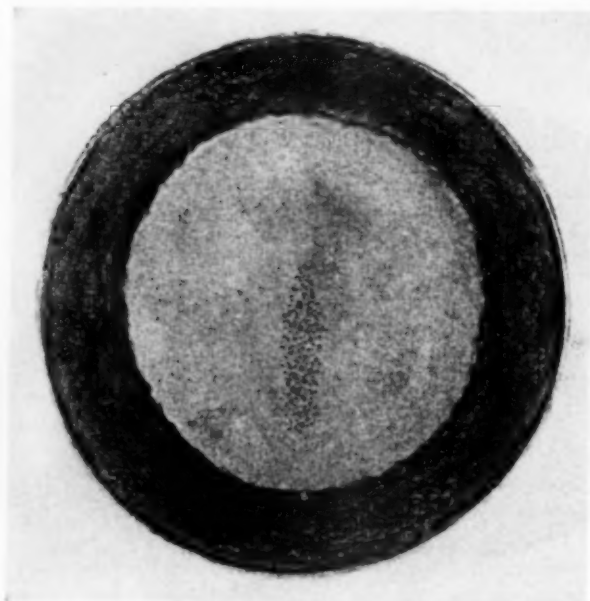


Fig. 11 (Calhoun). *Case 4.* Appearance of the Krukenberg's spindle of the left eye as seen in ophthalmoscopic light. (Compare with Figure 9.)

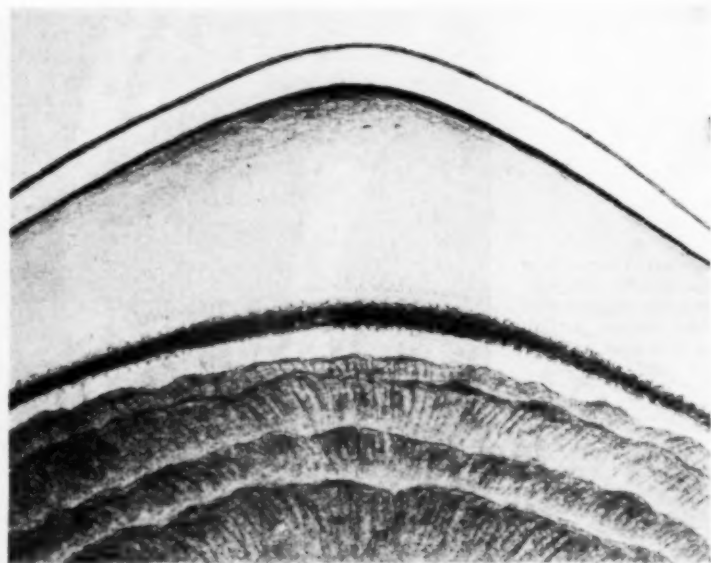


Fig. 12 (Calhoun). *Case 4.* Gonioscopic appearance of left eye, showing the narrow dense band of pigment in the trabeculum. The ciliary-body zone is wide and gray in color.

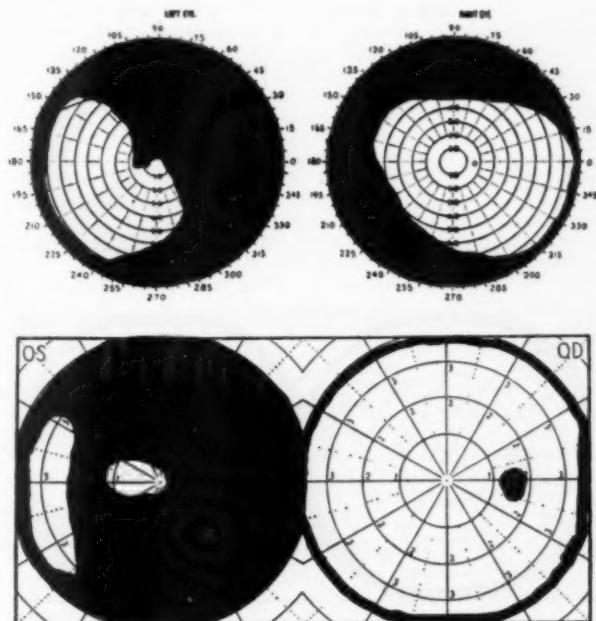


Fig. 13 (Calhoun). *Case 4*. Visual fields on March 5, 1949. Perimetric field with a 2/330 mm. test object; central field with a 2/1,000 mm. test object.

eye revealed complete atrophy of the pigment seam. The optic discs were small. The right nervehead was normal but the left showed moderate cupping and temporal atrophy.

Intraocular pressure was 43 mm. Hg (Schiotz) in each eye. Gonioscopy revealed a wide-angle entrance, a narrow and very dense brown pigment band in the trabeculum, and no trabecular synechias (fig. 12). Visual fields were normal in the right eye and showed advanced glaucomatous changes in the left eye (fig. 13).

The intraocular pressure was easily reduced to 20 to 25 mm. Hg (Schiotz) in each eye with miotics, but the resultant blurring of vision was so annoying that the patient requested operation.

On April 12, 1949, a successful trephination with peripheral iridectomy was performed on the left eye. Good subconjunctival filtration resulted and the intraocular pressure has remained 15 mm. Hg (Schiotz) ever since. Preoperative vision and field were maintained when last examined on May 24, 1952. Similarly, the right eye was operated upon on August 29, 1950.

In October, 1951, an acute conjunctivitis and infection of the trephine bleb developed in the right eye, but under local treatment this subsided without damage to vision or to the trephine bleb. The shape and degree of the posterior corneal pigment deposits have not changed in the three years since operation.

Neither tonography nor provocative tests were performed on this patient prior to surgery. Since operation, the pupils have been dilated with homat-

ropine on one occasion, but no free floating particles of pigment could be demonstrated in the anterior chamber.

The patient weighed 200 pounds and was five feet eight inches tall. He was in good general health but had received a thorough physical examination in March, 1947, because of the complaint of sterility of three years' duration. The physical examination revealed that he was overweight and that there was a "failure of accommodation" of the left eye. Urinalysis, complete blood count, and blood chemistry were all within normal limits. Basal metabolic rate was minus-one percent. An X-ray study of the skull revealed an abnormally small, partially closed sella turcica. Prostatic secretion revealed a sperm count with only a slightly subnormal number of mobile sperm. He was given small doses of thyroid and two months later reported that his wife had become pregnant.

CASE 5

A 23-year-old man who had first noted halos around lights in January, 1949, and a defect in the visual field of the right eye since April, 1949, was found to have glaucoma in July, 1949. A trephination with complete iridectomy was performed on the right eye and two weeks later a trephination with peripheral iridectomy was performed on the left eye.

Two weeks later on August 17, 1949, when first seen by me, the vision in the right eye was 20/30 with -2.0D. sph. \ominus -0.5D. cyl. ax. 165°, and in

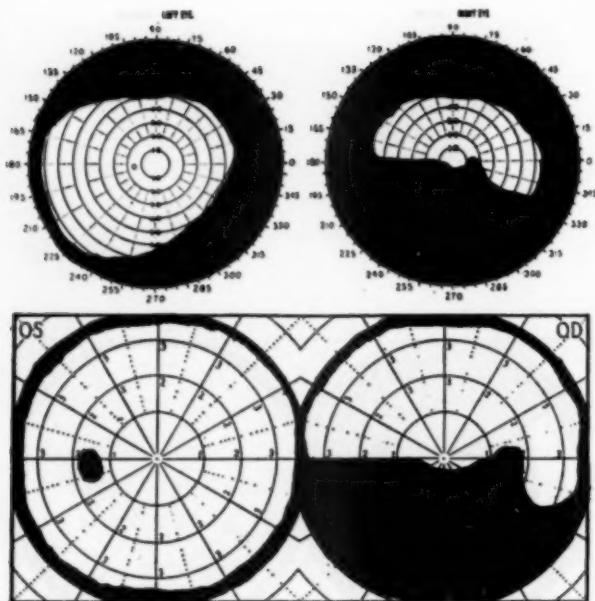


Fig. 14 (Calhoun). *Case 5.* Visual fields on August 17, 1949. Perimetric field with a 3/330 mm. test object; central field with a 3/1,000 mm. test object.

the left eye, 20/20 with $-1.0D.$ sph. $\ominus -0.75D.$ cyl. ax. 75° .

The right eye showed good subconjunctival filtration superiorly and the left eye very little filtration. The patient's hair color was red and the iris color was light brown.

Just below the center of the pupil on the back of each cornea could be seen a fine vertical pigment spindle which was about the same size in each eye. Both optic discs showed marked glaucomatous cupping. Intraocular pressure was 15 mm. Hg (Schiotz), right eye, and 22 mm. Hg, left eye.

Visual fields were normal in the left eye and showed marked changes in the right eye (fig. 14).

Gonioscopy performed later revealed an anterior chamber of normal depth, an open filtration angle, and no trabecular synechias except at the edge of the operative sites. A dense ring of pigment could be seen in the trabeculum.

The intraocular pressure was found to fluctuate markedly and to be greatly affected by emotional upsets. In November, 1949, another trephining operation was performed on the left eye. This controlled the tension for a few months but in October, 1950, the tension of the left eye persisted at 40 mm. Hg (Schiotz). On October 23, 1950, the vision in the right eye was 20/20 with $-2.5D.$ sph. $\ominus -0.5D.$ cyl. ax. 165° , and in the left eye, 20/20 with $-2.0D.$ sph. $\ominus -0.75D.$ cyl. ax. 75° .

On October 25, 1950, a trephining with peripheral iridectomy was performed on the left eye. A severe intraocular hemorrhage followed the operation and the vision was reduced to 20/70.

In September, 1951, the tension became elevated again in both eyes, and a trephining operation was

performed on the right eye on September 5, 1951. Severe anterior chamber and vitreous hemorrhage followed this operation reducing the vision to 20/100 without lowering the intraocular pressure. When last seen in November, 1951, the vision was reduced to 20/200 in the right eye, 20/100 in the left, intraocular pressure was 55 mm. Hg (Schiotz) in the right eye and 27 mm. Hg in the left eye. Old blood was still present in the vitreous cavity of both eyes, and to a slight degree in the anterior chamber of the right eye. The pigment spindles on the posterior surface of the cornea had not changed in size from the original examination.

The patient was six feet one and one half inches tall and weighed 200 pounds. Until about one year before the onset of the glaucoma, the patient had been on a forced fluid intake and vitamin A (25,000 units, daily) for four years because of an acne of the face. The patient was in good general health but under much emotional tension and strain. General physical examination, urine examination, and blood chemistry determinations were all normal. X-ray examination of the skull revealed a normal sella turcica and an area of fibrous dysplasia in the left frontal region.

CASE 6

A 37-year-old white man was first seen on February 8, 1952, complaining of poor vision in the left eye since about January 1, 1952. The patient's mother had advanced glaucoma. The patient was in good general health, was six feet one and one half inches in height, and weighed 200 pounds. A recent general physical examination was normal. The patient had been married four years but no

pregnancy had resulted. No examinations had been carried out to determine the cause of this. There were no other symptoms referable to the endocrine system.

Refraction revealed the vision in the right eye to be 20/20 with a $-0.5D$. sph. and in the left eye 20/100 with a $-0.5D$. sph. The patient's hair color was dark brown and iris color was blue-gray.

Corneal biomicroscopy revealed a well-marked vertical spindle of fine pigment on the posterior surface of each cornea. The spindle was largest and most dense in the left eye. The pigment seam of the iris showed considerable atrophy in the left eye but none in the right eye. The lens was clear. No pigment dots were seen on the iris surface.

Gonioscopy revealed a deep anterior chamber, a wide angle, and moderate pigmentation of the posterior trabeculum more marked in the left eye. The optic discs showed marked glaucomatous cupping and atrophy in each eye. Visual fields were normal in the right eye but showed a moderately advanced defect in the left eye (fig. 15). Intraocular pressure was 45 mm. Hg (Schjötz), right eye, and 55 mm. Hg left eye.

A mydriasis test performed with homatropine hydrobromide (two-percent solution) resulted in no change in intraocular pressure in one hour. A water provocative test was not performed. Measurement of the facility of aqueous outflow as determined by tonography with the electronic tonometer gave the following results: In the right eye the intraocular pressure became reduced from 32.0 mm. Hg to 27.9 mm. Hg, to give a "C" factor of 0.05. Tonography was not carried out in the left eye.

KRUKENBERG'S SPINDLES WITHOUT GLAUCOMA

CASE A

A 30-year-old white woman with no eye complaints and in good general health was found, upon routine examination, to have mild Krukenberg's spindles. Vision, right eye, was 20/30 and, left eye, 20/70. Refraction revealed: R.E., $-0.25D$. sph. to give 20/15; L.E., $-0.75D$. sph. $\ominus +0.25D$. cyl. ax. 180° to give 20/15. The patient had dark hair and the iris color was blue-gray.

Corneal biomicroscopy revealed a faint vertical

collection of fine pigment on the posterior surface of each cornea. This pigment collection could not be detected with ophthalmoscopic light. There was no atrophy of the pigment seam of the iris and no pigment deposition on the iris.

Gonioscopy revealed an open angle without synechias. The trabeculum showed only very light pigmentation. Intraocular pressure was 15 mm. Hg (Schjötz) in the right eye and 16 mm. Hg in the left.

Following full dilatation with homatropine hydrobromide (two-percent solution) the tension rose only to 17 mm. Hg in the right eye and 20 mm. Hg in the left eye. During a one-hour period following the ingestion of one quart of water on an empty stomach the tension rose to 20 mm. Hg in the right eye and 23 mm. Hg in the left eye.

Tonography, as measured with the electric tonometer, gave the following results: In the right eye the initial pressure was 11.9 mm. Hg (Schjötz) and four minutes later was 9.8 mm. Hg to give a "C" factor of 0.06; in the left eye the tension initially was 13.8 mm. Hg (Schjötz) and four minutes later was 9.4 mm. Hg to give a "C" factor of 0.13.

It can be seen from data given above that the results of the provocative tests were all negative in this case.

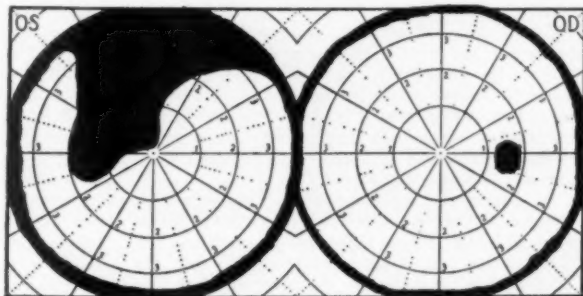
CASE B

A 40-year-old white woman, in good general health, was first seen in January, 1951, complaining of inflammation and scratchy sensation in the right eye. She was found to have a mild superficial punctate keratitis in the right eye which has subsequently been very resistant to all forms of treatment. During the course of the examination, the patient was found to have a well-developed Krukenberg's spindle on the posterior surface of each cornea. The patient's myopia began rather suddenly 12 years previously following birth of her second child.

Refraction revealed a vision of 20/25 in the right eye with $-1.5D$. sph., and 20/20 in the left eye with $-1.50D$. sph. The patient had brown hair and the iris color was dark brown.

With oblique illumination and loupe, a prominent brown vertical spindle of pigment could be seen on

Fig. 15 (Calhoun). Case 6. Visual fields on February 29, 1952. Central field with a 2/1,000 mm. test object.



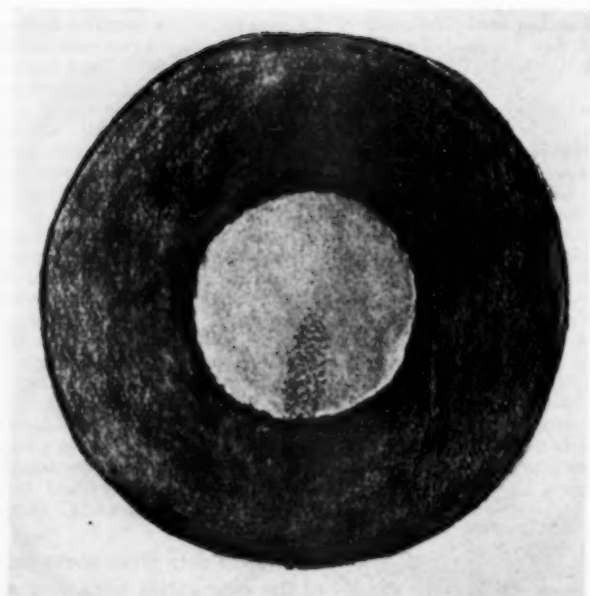


Fig. 16 (Calhoun). Case B. Appearance of the Krukenberg's spindle in the left eye as seen in ophthalmoscopic light.

the posterior corneal surface in each eye. The upper end of the spindle was slightly temporal in each eye. In ophthalmoscopic light, the spindle was less evident (fig. 16).

Corneal biomicroscopy revealed mild superficial punctate keratitis in the right eye. There was a large triangular area of closely packed dots of fine pigment on the posterior surface of each cornea (fig. 17). Inferiorly in both eyes at the termination of Descemet's membrane, the pigmentation was also evident. The iris surface was covered with scattered dots and flecks of brown pigment.

There was slight atrophy of the pigment seam temporally in the right eye and marked atrophy of the pigment seam over a wide area inferiorly in the left eye. The posterior corneal pigmentation and the prominence of the spindle were slightly greater in the right eye.

Following dilatation of the pupils a meridional line of light brown pigment could be seen on the inferior surface of the lens just posterior to the equator.

Gonioscopy revealed a wide angle without trabecular synechias. There was heavy pigmentation of the trabeculum all around, and inferiorly scattered pigmentation extended onto the cornea beyond Schwalbe's line (fig. 18). Ophthalmoscopic examination revealed the fundi to be normal. Intraocular pressure was 20.5 mm. Hg (Schiotz), right eye, and 20.1 mm. Hg, left eye.

At a later date the determination of the rate of aqueous outflow by means of tonography as measured with the electric tonometer revealed the following: From an initial pressure of 20.5 mm. Hg (Schiotz) in the right eye, the pressure after four

minutes was 11.2 mm. Hg, giving a "C" factor of 0.3. From an initial pressure of 14.6 mm. Hg (Schiotz) in the left eye, the pressure after four minutes was 10.0 mm. Hg, giving a "C" factor of 0.15.

Following the ingestion of a liter of water on an empty stomach, the intraocular pressure in the right eye rose in 45 minutes from an initial pressure of 17.2 mm. Hg (Schiotz) to 29.3 mm. Hg; and in the left eye from 13.8 mm. Hg (Schiotz) to 25.2 mm. Hg.

On another occasion homatropine hydrobromide (two-percent solution) was instilled into both eyes. Although full pupillary dilatation was produced, no change occurred in intraocular pressure when checked at intervals of 15 minutes for one hour. During the mydriasis test no free floating pigment particles could be detected in the anterior chamber by biomicroscopy.

In this case the only positive results were those obtained in the water provocative test in which the intraocular pressure of each eye became practically doubled.

CASE C

A white woman was first seen in 1943 at the age of 52 years. Refraction at that time revealed 20/25 vision in each eye with a -3.0D. sph. \ominus -0.75D. cyl. ax. 180° in the right eye; and -2.0D. sph. \ominus -0.75D. cyl. ax. 180° in the left eye. Krukenberg's spindles were noted at this time in each eye. The fundi were normal but there was considerable hyalitis in the right eye.

Fig. 17 (Calhoun). *Case B*. Biomicroscopic appearance of the left cornea to show that the pigmentation on the posterior corneal surface extends over a wide area.

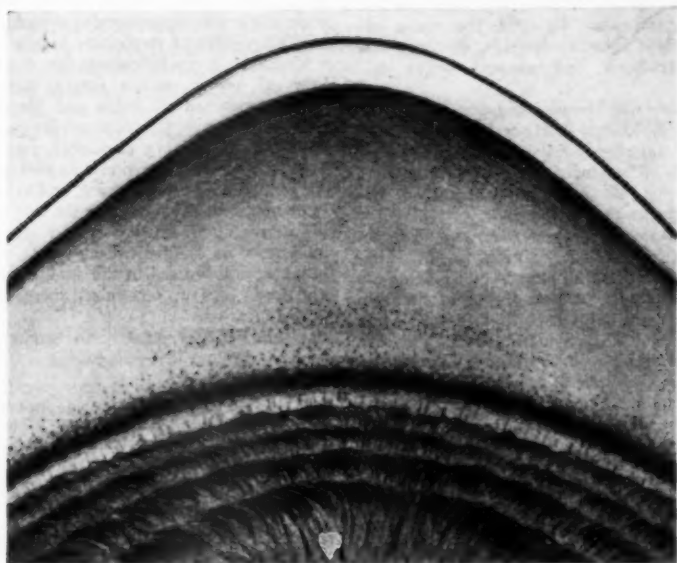
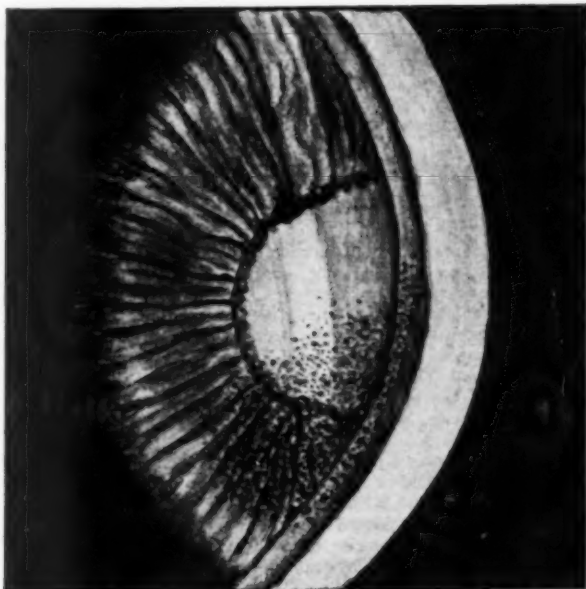


Fig. 18 (Calhoun). *Case B*. Gonioscopic appearance of the left eye, showing pigment deposition chiefly in the posterior portion of the trabeculum. Pigment is seen on the cornea anterior to the line of Schwalbe. The ciliary-body band is light purple in color.

The patient was next seen on February 21, 1951, complaining of gradual impairment in the vision of the right eye since early 1950 and of sudden loss of vision in that eye in October, 1950, following a light blow to the right temple by a rake handle. Diabetes mellitus was first discovered in December, 1951.

Examination revealed an extensive detachment of the retina inferiorly in the right eye with a reduction of vision to hand movements. Corrected vision in the left eye was 20/25.

Biomicroscopy revealed a collection of fine brown pigment dust on the posterior surface of each cornea, more marked in the right eye. This pigment formed a definite vertical spindle of which the upper end was directed slightly temporally. The anterior chambers were very deep. The iris color was dark brown. There was no atrophy of the pigment sear. A few flecks of pigment could be seen on the iris surface. No pigment deposits were seen on the anterior capsule of the lens.

Following dilatation of the pupils a concentric ring of pigment could be seen on the posterior surface of the lens just behind the equator; in the right eye it was most marked temporally and in the left eye nasally. The interior of the left eye was normal except for mild hyalitis. There was no diabetic retinopathy.

Gonioscopy revealed in each eye a similar heavily pigmented trabeculum without trabecular synechias. Intraocular pressure was 16.1 mm. Hg (Schiotz), right eye, and 16.9 mm. Hg, left eye.

Operation on February 27, 1951, was unsuccessful in restoring the detached retina of the right eye and when last seen on May 31, 1952, the vision remained reduced to hand movements, the lens was becoming cataractous and showed slight iridodonesis.

Full dilatation with homatropine hydrobromide (two percent) in March, 1951, and again in May, 1952, produced no change in the intraocular pressure as measured tonometrically during the hour following the test. No free pigment could be detected in the aqueous during the test.

On two occasions a water provocative test was performed, under the usual conditions of measuring the intraocular pressure at intervals following the ingestion of a liter of water on an empty stomach. In the right eye the tension on February 9, 1952, rose from 16.1 mm. Hg (Schiotz) to 25.7 mm. Hg (a rise of 9.6 mm. Hg) and on May 31, 1952, from 15.9 mm. Hg to 26.3 mm. Hg (a rise of 10.4 mm. Hg). In the left eye the tension on the first date rose from 16.9 mm. Hg (Schiotz) to 20.3 mm. Hg (a rise of 3.4 mm. Hg) and on the second date rose from 15.6 mm. Hg to 21.8 mm. Hg (a rise of 6.2 mm. Hg).

Determination of the facility of aqueous outflow as measured by tonography with the electric tonometer revealed the following: In the right eye an initial pressure of 22.8 mm. Hg (Schiotz) was reduced to 13.6 mm. Hg after four minutes, to give a "C" factor of 0.25. In the left eye an initial

pressure of 15.6 mm. Hg (Schiotz) was reduced to 8.5 mm. Hg to give a "C" factor of 0.25.

The glaucoma provocative tests and measurements of the facility of aqueous outflow were all negative in this case except for the positive water test in the right eye. The result obtained was probably related to the retinal detachment and iridodonesis rather than to the problem of pigment deposition in the trabeculum.

CASE D

I am indebted to Dr. Ralph S. Riffenburgh, Lt. MC, ESNR, who has kindly given me permission to include this case. A 22-year-old white man was seen with the complaint of blurring of vision. Vision was 20/70, right eye, and 20/30, left eye. Refraction revealed: O.D., -2.25D. sph. \ominus +1.75D. cyl. ax. 180° to give 20/15; O.S., -1.0D. sph. \ominus +1.0D. cyl. ax. 180° to give 20/15.

Ophthalmoscopic examination revealed some degree of haziness of the right cornea. Corneal biomicroscopy showed a typical vertical Krukenberg's spindle on the posterior surface of the right cornea, some six mm. in length. The left cornea showed a few pigment flecks, but not enough to form a spindle. The iris color was blue-green. Intraocular pressure was 25 mm. Hg (Schiotz) right, and 20 mm. Hg left eye. Central and peripheral visual fields were entirely normal. Gonioscopy revealed a wide angle with no trabecular synechias. There was moderate pigment deposition in the trabeculum.

One-half hour following the ingestion of one liter of water on an empty stomach the patient complained of halos and blurring of vision of the right eye. The intraocular pressure at this time was 40 mm. Hg (Schiotz), right, and 32 mm. Hg, left eye. The tension subsided promptly upon the instillation of pilocarpine, and at no time was it later elevated, even without the use of pilocarpine.

An intentional mydriasis test has not yet been performed on this patient. However, mydriatics had been previously used in the study of his eyes without producing any recognized increase in the intraocular pressure.

Urinalysis was negative for sugar.

CASE E

A 47-year-old white man was first seen on February 16, 1951, with a history of a persistent defect of the upper visual field in the right eye since an attack of acute optic neuritis in 1933. Krukenberg's spindles were discovered in both eyes at that time.

Examination revealed the vision of the right eye to be 20/30 with a -1.25D. sph. \ominus +2.5D. cyl. ax. 180°, and of the left eye, 20/30 with a -2.0D. sph. \ominus +2.25D. cyl. ax. 180°. The patient's hair color was dark brown and the iris color was steel blue or gray.

A prominent narrow vertical spindle of pigment was seen on the posterior corneal surface in each eye. Each spindle was slightly oblique, so that its upper end was more temporal than the lower end.

Biomicroscopy revealed a wide triangular area of fine pigment on the posterior cornea, more marked in the right eye. There was marked atrophy of the pigment seam of the iris and many dots and flecks of pigment could be seen on the surface of the atrophic iris. Many dots of pigment were deposited on the anterior lens capsule in the pupillary area. There was incipient cortical cataract in both eyes.

Following dilatation of the pupils pigment could be seen deposited on the posterior surface of the lens inferiorly behind the equator. The right optic disc revealed marked temporal pallor; the left disc was normal. There was a marked defect in the right upper visual field.

Gonioscopy revealed a deep anterior chamber, an open angle, and a rather dense pigment ring in the trabeculum of each eye. Intraocular pressure was 20.1 mm. Hg (Schiotz) in the right eye, and 19.5 mm. Hg in the left eye.

Following the ingestion of a liter of water on an empty stomach, the intraocular pressure rose only

to 23.4 mm. Hg (Schiotz) in the right eye and to 22.8 mm. Hg in the left eye when checked every 15 minutes for one and one half hours. At a later date pupillary dilatation was produced with homatropine hydrobromide (two-percent solution) but essentially no change was produced in the intraocular pressure when measured every 15 minutes for one hour. No free-floating pigment particles could be detected in the anterior chamber during the dilatation.

Measurement of the facility of aqueous outflow as recorded during tonography performed with the electronic tonometer revealed the following: In the right eye the initial pressure of 18.5 mm. Hg (Schiotz) became reduced in four minutes to 13.8 mm. Hg to give a "C" factor of 0.13; in the left eye an initial pressure of 15.6 mm. Hg became reduced to 11.0 mm. Hg to give a "C" factor of 0.15.

In this patient with Krukenberg's spindles and a history of old intraocular inflammation, glaucoma provocative tests were negative and tonography showed a normal facility of aqueous outflow in each eye.

478 Peachtree Street (3).

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OPHTHALMIC MINIATURE

Shading of the eyes and dilatation of the pupils by a drop of the solution of atropine every second night constitute the palliative treatment of cataract. Not merely in the incipient stage, but even in the advanced, many patients find their sight so much improved by these simple means, that they defer, for months or years, to submit to any surgical operation.

William M'Kenzie,
A Practical Treatise on the Diseases of the Eye,
Fourth Edition, 1854, p. 766.

TAPETORETINAL DEGENERATION

REPORT OF FOUR CASES OF A RARE FORM OF LUMINESCENT CRYSTALLINE TAPETORETINAL DEGENERATION: WITH A DISCUSSION OF ITS CAUSE

J. LIJÓ PAVÍA, M.D.

Buenos Aires, Argentina

REPORT OF CASES

CASE 1

E. C. L., a man aged 49 years, was first examined on August 4, 1941. Family history was negative. His mother, at the age of 105 years, was in good health. His four children had normal eyes. Formerly an excessive smoker, he used to smoke 30 leaf cigarettes daily, he now smokes only a pipe.

Laboratory examinations showed blood pressure to be normal. Wassermann and Kahn tests were positive. Blood cholesterol, 1.85 gm. percent; neutrophils, 62 percent; eosinophils, two percent; lymphocytes, 31 percent; monocytes, five percent.

Fundus examination with ordinary light showed:

Right eye. The disc was pale with no excavation and clear outer edges except in the right inferotemporal sector where the edge was slightly blurred. The caliber of the vascular branches was narrow. There was extreme atrophy of the retina and choroid, greater in the inferotemporal sector where

the choroidal vessels were pale or obliterated.

The macula had lost its anatomic configuration (fig. 1); only the external layers remained. Under the internal limiting membrane, a brilliant plaque seemed to be formed by many irregularly distributed, iridescent crystals which appeared to be crystals of cholesterol. In the center of the macular zone were two pigmented areas, perhaps residues of the pigment epithelium.

Left eye. The findings in the left eye (fig. 1) were essentially the same as in the right. Four nuclei of cholesterol deposits in the macula were independent of each other but trailed faint lines of luminescent, iridescent crystals and showed birefringent points.

Vision was: R.E., 1/25; L.E., 1/20.

There was greatly decreased dark adaptation and recognition of color.

The patient was given an intense course of mercury and bismuth therapy (1941) and, after two months showed some improvement, with vision of: R.E., 1/8; L.E., 1/10. This improvement in vision was still present when the patient was examined a year later, at

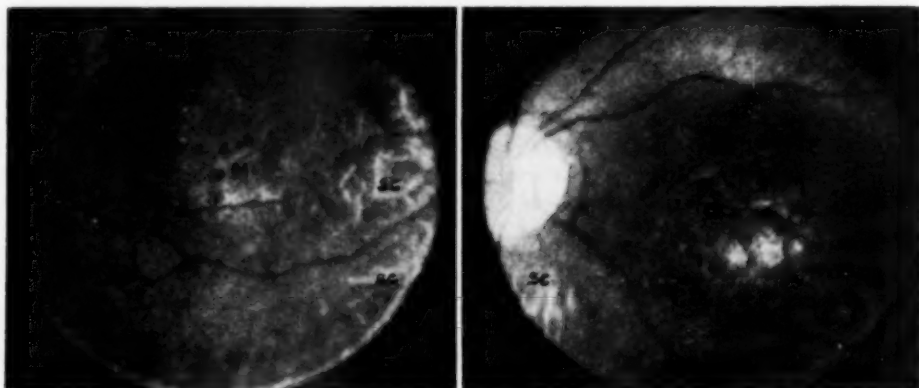


Fig. 1 (Lijó Pavía). Case 1. (Left) Retinograph of right eye: (M) Macula; (SC) Sclerosis of choroid. (Right). Retinograph of left eye: (SC) Sclerosis of choroid.

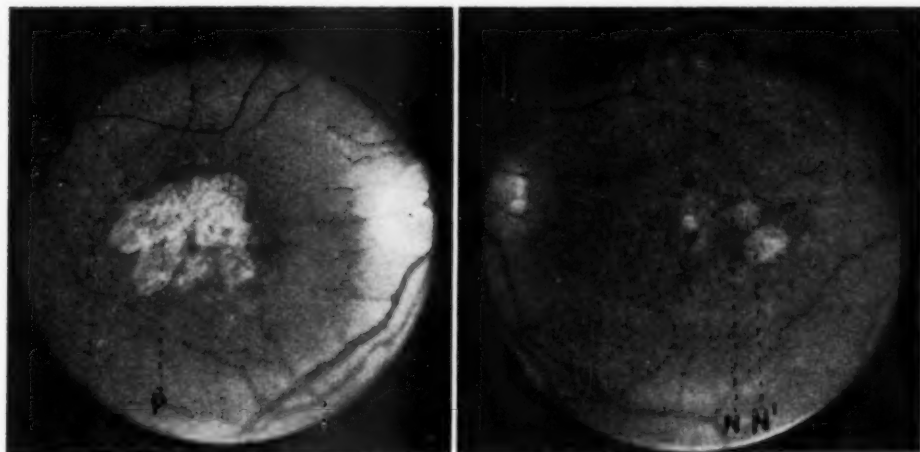


Fig. 2 (Lijó Pavía). Case 2. (Left) Retinograph of right eye: (P) Iridescent crystals. (Right) Retinograph of left eye: (N-N') Discock nucleus of crystals.

which time fundus examination of the right eye showed the crystalline plaque to be less prominent, and of the left eye, the plaques to be broken up and less luminescent.

CASE 2

A. N., a man aged 55 years, was examined on March 18, 1935. Family history revealed that his grandmother had heterochromia and one of his brothers, who lived abroad, had some ocular affection, the nature of which was not known.

For 10 years before this examination, the patient had noticed that he could not fixate his central vision. This difficulty had been diagnosed elsewhere as "macular choroiditis" of unknown etiology.

Although several Wassermann tests were negative at this time, the patient was subjected to intense antisyphilitic therapy.

The patient had been able to drive his car until three years ago when decreasing vision and marked diminution of the visual fields forced him to give up this activity. He had been told that his eye condition would progress slowly, but not to the point of blindness. This man also suffered from gastrointestinal disorders, and he had noticed that, with an increase in this trouble, his ocular

pain increased and his visual acuity diminished.

Examination of the fundus with ordinary light showed:

Right eye. The disc and vascular system appeared normal (fig. 2); in fact, both vascular and arteriolar distribution seemed perfect in the macular region. However, an irregular, lobulated plaque with several luminescent crystals which appeared iridescent when the light intensity was changed, was present in the macula. Some small vessels and pigmented spots could be seen on the lesion.

Left eye. The macular lesion is divided into small sectors (fig. 2), three of which are of an irregular discock shape; several crystalline points overflow into the rest of the macular region.

With the aid of the Aneritra light, it was possible to see the internal limiting membrane in both eyes. It presented a mirrorlike appearance and was mosaic in form. Also visualized were the internal layers of the retina through which passed the small vessels of the macular periphery.

The rest of the retina had disappeared, as well as the choriocapillaris, and was replaced by a cottonlike tissue impregnated with crys-

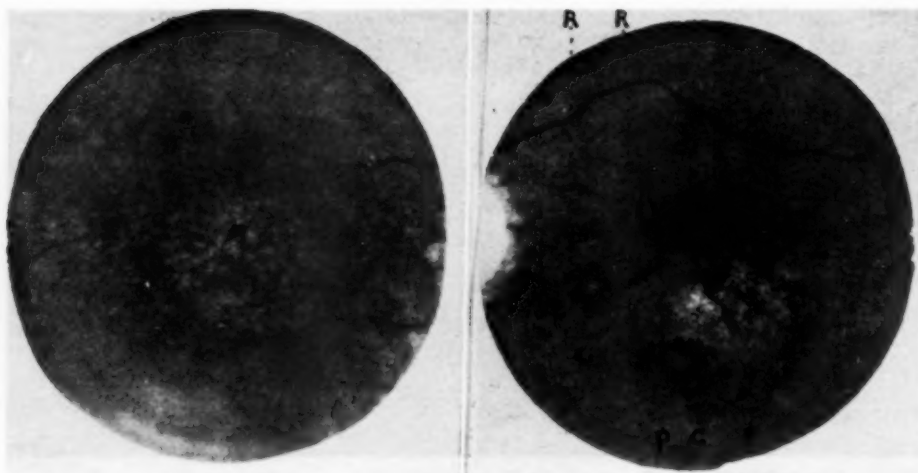


Fig. 3 (Lijó Pavia). Case 3. (Left) Retinograph of right eye. (Right) Retinograph of left eye: (R-R) Slight reflexes of double outline. (P-P') Macular lesion. (C) One nucleus of a mirrorlike corpuscle.

tals (cholesterol). Around the disc was a ring of atrophy where obliteration of the medium vessels of the choroid started.

Vision was: O.U., 1/10. Dark adaptation (Lijó Pavia adaptometer) showed: R.E., one fourth of normal; L.E., one half of normal. Color vision (Stilling tables) showed loss of red and green sense.

Laboratory tests showed increased eosinophils (nine percent) and the presence of *Blastocystis hominis* (vegetative form) and *Endamoeba histolytica*. On the basis of these findings, an adequate treatment was prescribed.

CASE 3

A. M., a man aged 28 years, was examined on April 30, 1942. Family history was negative. After working for three years as a glass maker, his ocular difficulties had been diagnosed as "burns of the cornea." Later, he had worked for three years, firing crystal particles with a flame 15 cm. in length produced by a torch with a one-cm. diameter. For the past four years, he had worked in a room 2.0 by 3.0 meters where the glass articles were fired under such intense heat that, even 24 hours after the heat had been turned off,

gloves had to be used to touch the articles.

For six years vision had decreased progressively and several doctors had given reserved diagnoses, one of which was choroiditis. Tests for syphilis had been negative. Methyl antigen had been used.

Examination of the fundus under ordinary light showed:

Right eye. The temporal half of the disc was very pale and surrounded by a bright green ring, wider at the upper and outer edge. The arterioles showed calibers one third of normal. Brief vertical reflexes of the internal limiting membrane could be seen between the disc and the macula. The macula itself was completely covered and even exceeded by a plaque of undefined outline, roughly circular, which was formed by an infinite number of brilliant luminescent points which reflected different colors but showed a predominance of bright green (ophthalmoscopy). See Figure 3.

The arterioles and small veins which could be seen at the periphery of the macula were lost among the crystalline points at the under-surface. With the Aneritra light, it was possible to observe the mass of crystals (or bright particles) better and it was seen that

a yellow substance was spread over the entire plaque and the peripapillary ring of bright green appeared as a slight exudation of the internal retina. In the perimacular region were slight reflexes of double outline.

Left eye. The same peripapillary, macular, and papillomacular appearance was observed (fig. 3). However, the lesion was divided into two sectors by an irregular and slightly oblique line of pigment. The base of the internal sector was on this dividing line and three regular sides formed of numerous bright crystals separated the undamaged retina and the atrophic lesion. The external sector was dotted with irregularly distributed mirrorlike corpuscles which, in some places, overflowed the macula. Under Aneritra light, the yellow substance appeared to be faintly disseminated in the core of the lesion.

Biomicroscopic examination verified the belief that the macular lesion was not compact. By varying the angle until the brilliant green reflection was obtained, it was possible to see tiny holes through which the pink color of the choroid could be seen, as well as very small vessels running across the spongy mass formed by the juxtaposition of the crystals. Along the course of these tiny vessels the reflections were interrupted.

Vision was greatly diminished. It was impossible to test dark adaptation and color

vision and to take visual fields.

Laboratory tests revealed: Eosinophils, nine percent; cholesterol, 2.33 gm. percent. Insulin and diabetic treatment were recommended.

One year after therapy was instituted, examination showed cholesterol to be 1.70 gm. percent and vision, O.U., 1/6. The fundus examination revealed small red sectors on the macula, and, under Aneritra light, the yellow substance showed greater intensity. Under sodium light, a greater separation between the crystals could be observed.

Biomicroscopic examination ($\times 54$) with polarized light seemed to bring out the phenomenon of birefraction but the focus on the crystals was uncertain.

Insulin treatment was continued and cholesterol continued to be controlled. Vision, O.U., increased to 1/10 and remains 1/10 after two years.

CASE 4

M. G. L. G., a woman, aged 33 years, married for 11 years but childless, was first seen in September, 1941. Her family history was negative. When she first noticed decrease of vision at the age of 18 years, she was told no fundus lesion was present. Further progressive reduction in vision and the presence of a central scotoma caused her to consult

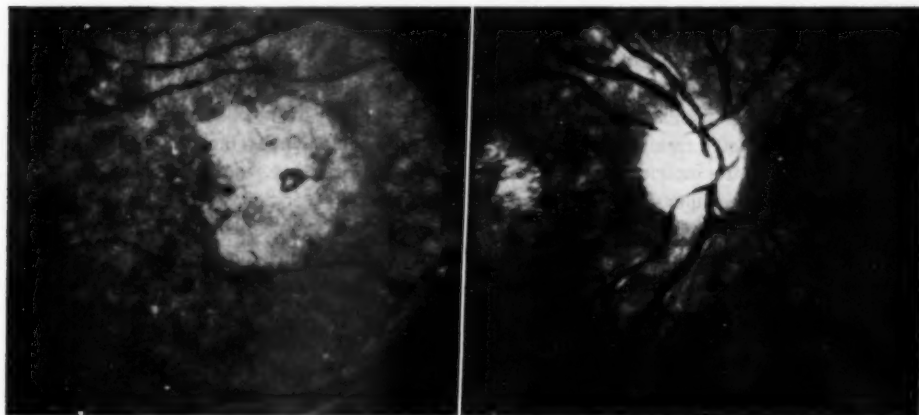


Fig. 4 (Lijó Pavia). Case 4. (Left). Retinograph of right eye, showing lesion of the macula and surrounding white spots. (Right) Retinograph showing papilla surrounded by white spots.

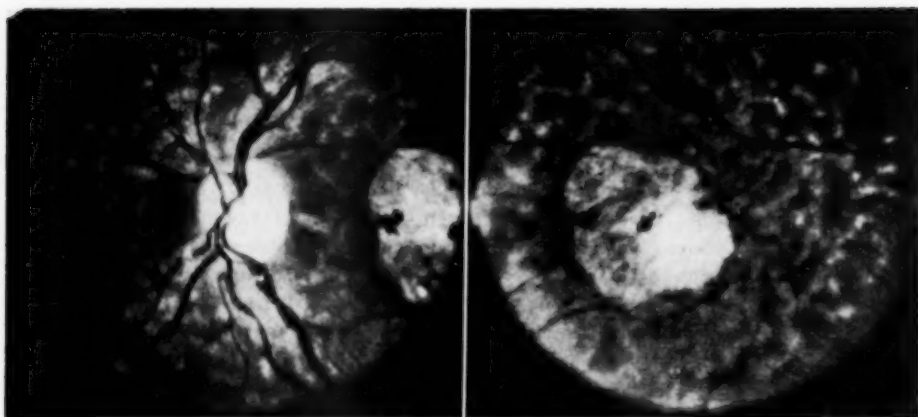


Fig. 5 (Lijó Pavia). Case 4. (Left) Retinograph of left eye, showing papilla surrounded by white spots. (Right) Retinograph showing macular lesion surrounded with many small white spots.

other specialists and her condition was finally diagnosed as Stargardt's disease. Uterine malformation was the cause of her sterility. She had also been under long treatment for an intestinal disorder.

Fundus examination (figs. 4 and 5) in ordinary light showed:

The ophthalmoscopic aspect of both eyes was similar. There was slight pallor in the temporal half of the disc and slight enlargement of the physiologic excavation. With the exception of the macula, the distribution of the blood vessels appeared normal. At the left macula, only three arterioles and small veins could be seen; on the right, scarcely one. There was slight reduction in the caliber of the arterioles. The lesions of both maculas were similar. There was absence of foveal, macular, and perimacular reflexes, with atrophy of the greater number of the layers of the retina, only the internal limiting membrane and the nerve-fiber bundle remained, and these in a degenerated state.

Considered in their entirety the macular lesions extended beyond the limits of the macula itself, forming two irregular plaques, with meeting edges, straight in some places and dented in others. The bases of both plaques seemed to be formed by pigment epithelium. A cottonlike substance, several segments of white chords (probably obliterated choroid vessels), and dispersed pigment

cells were piled in an atypical mass in each macula and were partly covered by innumerable disseminated corpuscles of luminescent crystals (cholesterol).

In both eyes (figs. 7 and 8), the posterior pole of the fundus showed a singular aspect. Surrounding the disc, the macular, and the papillomacular sector were series of little white spots which in some places joined to form irregular figures; some were spread here and there in branches in the right eye, but showed a more orderly distribution in the left eye.

The surface upon which these white spots appeared, extended for two disc diameters over the papilla and macula, two disc diameters on the outer side, and one and one-half disc diameters on the nasal side. Many of them could also be observed in the papillomacular sector (fig. 6). Several examinations with the direct-image and with binocular ophthalmoscope verified their location in the depth of the retina behind the vessels in the most external retinal layers.

Examination with Aneritra light enabled one to see the points at which the plaque edges were slightly blurred, which was the case of most of the lesion in the right eye. Almost the entire outline of the plaque in the left eye was dented. A tenuous yellow spot, about the size of a normal macula, was also seen.

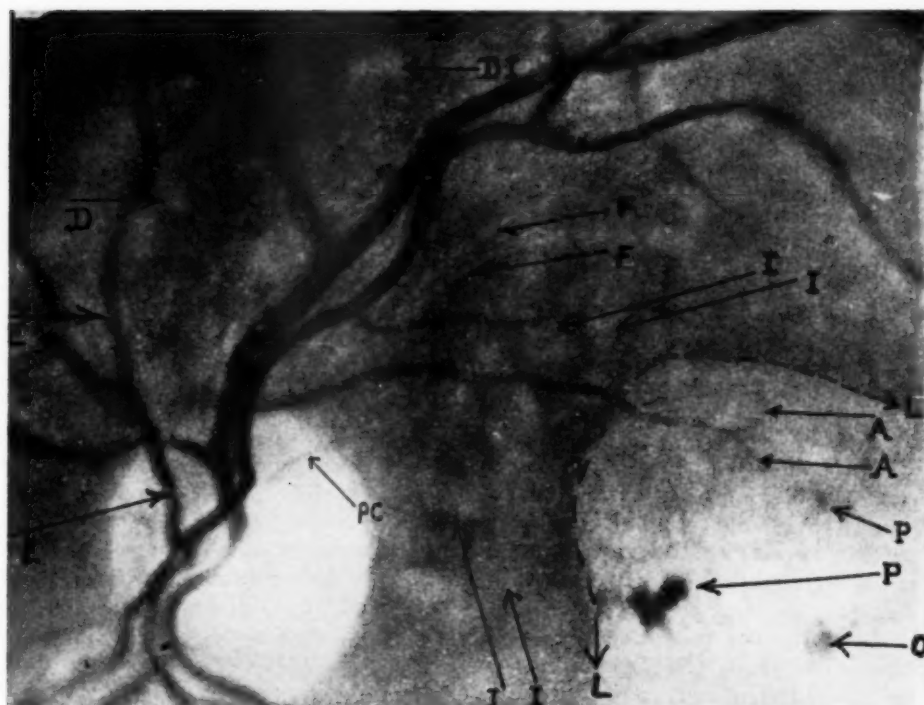


Fig. 6 (Lijó Pavía). Case 4. Left eye. High-power view of a small section from Figure 5.

(L-L) Interrupted line partially follows the outer edge of the macular lesion.

(P) Two pigmented masses.

(O) Optic center of retinograph.

(D) Drusen of the lamina vitrea.

(I) Noncompact substance located in the center thickness of the retina, together with the drusen (whitish spots) that surround the papilla, forms the plaque of macular degeneration.

(DI) To the left a drusen; to the right the whitish substance that is presumed to be cholesterol deposits.

(F) Nerve fascicles in the initial degeneration.

(E) Narrowing in the superior nasal arteriole.

(A) Probably precapillary vessels of the macular region.

(PC) Precapillary.

Biomicroscopic examination with the help of contact glasses showed that the macular lesions contained numerous polychromatic particles which reflected the light in a manner similar to that of a reflecting mirror. This reflection appeared at any point of the plaque at which the luminous focus was directed. Figure 9 shows an intensely white sector at different points.

It was possible to verify the observation that small vessels were present in the periphery of the macular plaques. Due to the disappearance of the external layers of the

retina, the pigment epithelium, and the choriocapillaris, the plaques appeared to be excavated on a plane behind the surrounding retina. The residues of these structures and the crystalline deposits were joined in a roughly faceted formation, similar to a reticulated tapestry. In some places, this formation showed spontaneous pulsations, synchronous with the radial pulse, of which I was able to make a cinematographic record.

Vision, greatly reduced, was: R.E., 1/25; L.E., 1/20.

Visual fields of the right eye, taken with a



Fig. 7 (Lijó Pavia). Stereoretinograph of right eye (Case 4).

Bjerrum screen and Best projector, showed a central scotoma extending irregularly up to eight degrees and a slightly enlarged blind-spot. It was only possible to obtain a 10/1,000 isopter: nasal, 27 degrees; temporal, 30 degrees; above, 18 degrees; below, 25 degrees.

Dark adaptation was moderately diminished. Color vision (Stilling's tables) was diminished for red and green.

Physical examination showed hepatic trouble and arterial hypotension.

Laboratory tests showed: Wassermann and Kahn, negative; cholesterol, 3.12 gm. percent.

After consultation with her physician, an intensive treatment of intravenous fibrolysin and potassium iodide was prescribed. Four months later, the patient showed improve-

ment with vision increased to 1/17, O.U. Visual fields and dark adaptation were also slightly improved and cholesterol was reduced to 2.0 gm. percent.

The treatment was continued for two years and the improvement maintained, with the cholesterol going below 1.90 gm. percent; the central scotoma decreasing to eight degrees in the right eye and seven degrees in the left and it was possible to use a 5/1,000 isopter. All meridians showed an increase of from five to eight degrees.

Early in 1944, this patient suffered intermittent arterial spasms in the papillary branches which were accompanied by momentary amaurosis and subjective color and light sensations. Blood pressure was 135/85 mm. Hg and pressure of the central retinal artery was 36 mm. Hg, indicating a good

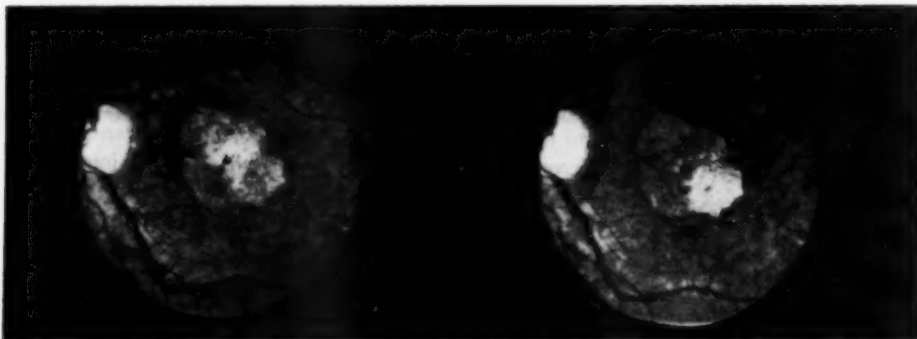


Fig. 8 (Lijó Pavia). Stereoretinograph of left eye (Case 4).

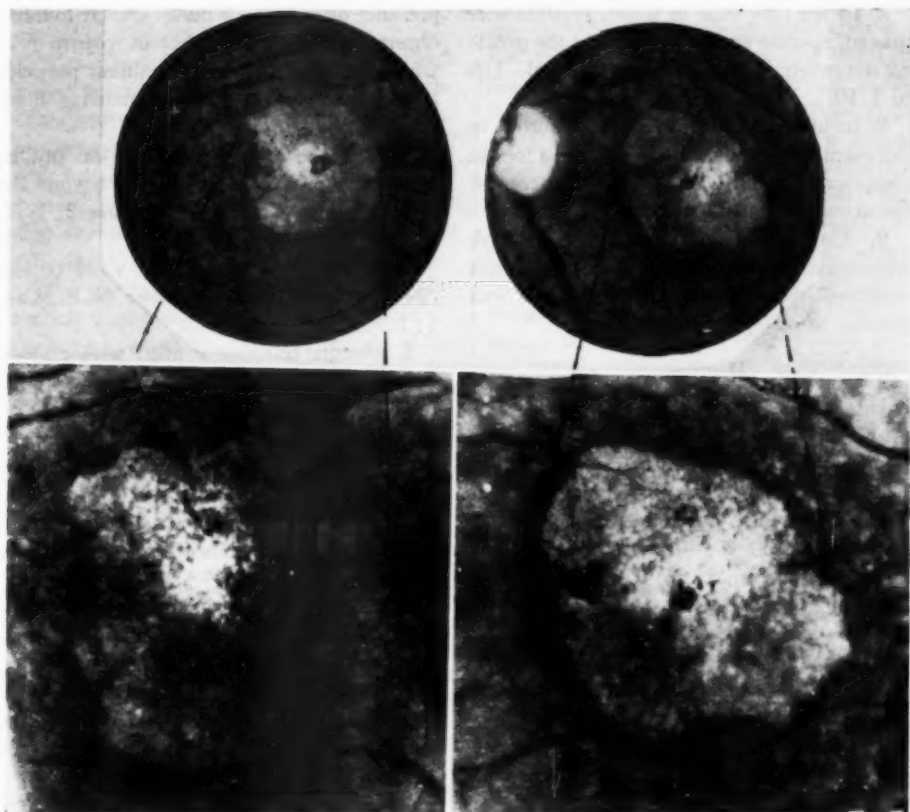


Fig. 9 (Lijó Pavía). Case 4. Enlargements of the retinographs of both eyes.

vascular condition. The heart findings were normal. Hormone treatment was intensified.

By the end of that year, the momentary amaurosis was occurring at more frequent intervals, the average three a month, accompanied by the appearance of blue spots and reddish lines. Cholesterol was at 1.60 gm. percent and vision was again decreased to 1/20, O.U. The patient was then lost to follow-up.

SUMMARY

There are similar characteristics in the four cases reported:

1. The essential lesion was situated in the macula, and each case showed the presence of brilliant luminescent crystals, probably

cholesterol in nature.

2. Direct vision did not exist in any case. One patient had vision of 1/10; two others had a low of 1/20; and the fourth had vision reduced to counting fingers at 30 cm.

3. In three cases, the symptoms appeared in adulthood; in one during adolescence.

4. In only one case was there a family history of ocular disturbance—a brother who lived in Europe and could not, therefore, be examined.

5. In no case were there inflammatory symptoms.

6. Hypercholesteremia was present in two cases which suggested an endocrine dysfunction. Hormone therapy brought improvement which lasted three years.

7. In the only case in which syphilis was proved, specific treatment brought the greatest improvement that could be expected—1/8 to 1/10.

8. In all cases, atrophy of the choroid in the macular region was observed as a logical complication of the degenerative process of the macula (Troncoso).

9. Alterations in color vision and dark adaptation were proved in three cases. It was observed in the fourth case but it was not possible to verify it.

DISCUSSION

In all of these cases, the choroidal-retinal atrophy was absolute and was characterized by the presence of luminescent crystalline bodies that formed a sort of tapestry in the lesion. Plaquelike, they were distributed in a more or less compact form and reflected light as if they were mirrors.

Bietti¹ reported several cases and pointed out the presence of crystals of cholesterol in a dispersed form in the external layers of the retina, with probable migration to the internal layers.

Wolflein and Lo Russo² interpret these same crystals as wartlike formations in the lamina vitrea upon which formations of cholesterol and calcium have been deposited.

Gayet³ suggests the transformation of the pigment epithelium and its probable cholesterol degeneration.

Other investigators have referred to the presence of these crystalline particles in dispersed form. Van Duyse⁴ describes the spotting of the perifoveal and polar areas with points of "diamondlike splendor" which he took to be crystals of calcium. Scotti⁵ mentions "points which reflected light intensely, giving the impression of small birefractile crystals."

Urrets-Zavalía refers to round, brilliant points, and Bussola⁶ speaks of round and luminous points. Koyanagi⁷ refers to the substitution of pigment epithelium by an impregnation of lipoid granules.

I have not found any reference to the

presence of plaques or nuclei similar to those observed in the cases herein reported in which conglomerations of brilliant particles have been identified in the following three forms:

1. A plaque of more or less clear outline which occupies or even extends beyond the macula (R.E., Case 1; R.E., Case 2; L.E., Case 3; O.U., Case 4).

2. Small nuclei of crystals, more or less disconnected from one another (L.E., Case 1; L.E., Case 2).

3. Macula completely filled with crystals having iridescent reflexes and without defined borders (R.E., Case 3).

As in cases of hereditary degeneration in which the polymorphism of the lesions was evident (François⁸ and Bietti⁹), so in the cases here reported. It would seem, therefore, that Bietti's conclusions are very much to the point:

"In degenerations which affect the external layers of the retina and the pigment epithelium, there are no set separations and it is possible to find association of different conditions in the same case. In such cases, this association is not exclusively in the macula.

"Narrowing of the vessels, retinal atrophy, and choroid disorders can coexist."

In my cases, although there was a history of ocular disorders in a sibling in one case (Case 2) which could not be investigated and therefore remains in doubt, it seemed the only justifiable classification was "acquired tapetoretinal degeneration." The hypothesis is suggested that, if the normal "lifetime" of the macula is limited by a peculiar fragility or predisposition or by imperfect development, a general toxicity, infection, or endocrine dysfunction may act upon this "point of lowest resistance." Franceschetti and co-workers refer to this in their remarkable study, *Heredity in Ophthalmology*.¹⁰ Bailliart in his chapter on the "Retina,"¹¹ also refers to "acquired degeneration" which would be senile degeneration of the macula and which is sometimes ac-

accompanied by intensive vascular sclerosis of the choroid (Lijó Pavia¹²).

With the exception of Case 3, in which vision was almost nil, it was possible in the cases here reported to verify the alterations in dark adaptation which, as has been pointed out by Marquez,¹³ were associated with central scotomas. Such alterations confirm that the lesion is neuro-epithelial in origin (Bonnet¹⁴).

The anatomic substratum of the tapetoretinal degeneration described by Renard¹⁵ includes: Transformation and atrophy of the pigment epithelium with migration of its elements, sclerosis of the vascular walls and narrowing of the caliber, and slow atrophy of the choriocapillaris.

The predominance of polar localization can be explained by what may be described as the "terminal circulation" of this region (Gonin¹⁶).

The most minute alteration in the pigment epithelium is sufficient to produce changes in dark adaptation. Lagrange,¹⁷ in his excellent report, admits that an acquired degenerative condition may be accompanied by color blindness.

The slight changes in color vision, especially for red and green, in my cases coincide with the observations of Bourdier and Shaaff¹⁸ that acquired disturbances generally are more simple in form than congenital ones.

In commenting upon the cholesteremia present in Cases 3 and 4, the question is posed: Can cholesteremia in itself produce retinal lesions?

Chauffard maintains (Redslob¹⁹) that such a condition produces circulatory troubles of suprarenal origin. Dubois-Poulsen does not accept this theory because other diseases, biliary, lithiasis, cholemia, xanthelasma, which do not produce retinopathies, co-exist with cholesteremia; inversely, there are retinopathies without cholesteremia.

Redslob refers to the case of a patient, aged 51 years, who showed a normal vision and fundus. Four years later she had a

typical myxedema, with a basal metabolism rate of -32 percent, hypercholesteremia of 3.40 gm. percent, and a macular degeneration with yellow foci and punctate hemorrhages. A central scotoma was present and vision was reduced to 0.2 and 0.5. Thyroid treatment was instituted and, two years later, the myxedema had disappeared, the basal metabolism rate was a -16 percent, and blood cholesterol was 1.80 gm. percent. Vision had neither improved nor grown worse; the central scotoma was approximately the same, and the degenerative macular lesions persisted but without hemorrhages.

In Redslob's opinion, the myxedema had produced the macular lesions. It seems to me that this opinion is correct and that the reason vision did not change in Redslob's case was because the entire retina was not affected by the degeneration, the more external layers remaining undamaged.

Finally, an attempt should be made to interpret the perimacular-papillary ophthalmoscopic findings in both eyes of Case 4. The exceptional extent of the lesions, the deposition of the white spots, their location in the retina, their form, size, and relation to each other gave them an uncommon interest. Franceschetti¹⁰ illustrates (figs. 6, 7, and 8¹⁰) a hyaline degeneration which in no way resembles my observations. Nor do the findings in my case resemble the disseminated white points seen in retinitis punctata albescentis, nor in guttata choroiditis—which processes may be classified as tapetoretinal degenerations.

If the retinographs that Pillat²⁰ illustrates in Plate 83, figs. 1, 2, and 4; Plate 84, fig. 1 are studied carefully, it must be concluded that the white spots seen in my Case 4 are what those of the German school would call "drusen of the lamina vitrea."

The three cases presented by Pillat show the drusen located in a large circle that surrounds and slightly exceeds the nasal side of the disc. The drusen are of different sizes, are not all round, are arranged in small lines

or in brief branching figures; in size and appearance they resemble those seen in my Case 4.

In order to confirm this interpretation, reference is made to an histologic section of drusen of the lamina vitrea in A. Fuchs²¹ in which the relation of the lesion to the pigment epithelium is illustrated. The size of the white spots shown by Fuchs closely approximates that of the white spots shown in my Figure 6(D, D).

Case 4 herein reported also resembled one illustrated by Bailliart in his Retinogram 77.²² Bailliart classified his case as one of "juvenile bilateral macular lesion" with a central scotoma and vision of 1/10. He describes the spots as "little yellow spots similar to those of capillaritis."

In a case of macular degeneration which I saw in 1932,²³ there were small refractile points around the macula and located in the external layers of the retina, which had the appearance of tiny pieces of gilt paper. Two years later, I reported^{24, 25} two cases, one of which showed a typical pigment degeneration with macular alterations, and the other a degeneration of the macula, around which 20 whitish spots could be observed, with probable involvement of the choroid.

In such cases, the pigment epithelium cannot but be involved and one must agree with Magitot²⁶ when he says:

"The pigment epithelium behaves like a gland annexed to the retina; it is a secretory epithelium that can replace its dead cells with newly formed elements by a process of direct division, capable of phagocytosis, of producing pigment and of losing it, and of producing hyaline substances and wartlike formations similar to what the German school calls drusen. Its capacity for proliferation is unlimited as is proved by discoid macular degeneration."

Magitot's microphotographs illustrate these words.

On the other hand, Bartolozzi²⁷ has observed some cases in which, in addition to the macular alteration, yellow spots (which he calls "drosas") were disseminated through the retina.

Carreras-Mata²⁸ states "this co-existence or successive transformation from one form to another induces one to suppose that the tapetoretinal degenerations are not simply a group of diseases of certain incidence and symptoms but rather may be different forms of a single disease."

The co-existence of two distinct processes in my Case 4 provide a certain evidence for the statement of Stadlin and Van Bogaert²⁹ that it is possible to observe ophthalmoscopic alterations inflammatory in type accompanying a degenerative process. By binocular ophthalmoscope, my Case 4 showed that, in front of the "drusen" and in the depth of the retina, the diffused mass that formed in part the white perimacular-papillary spots was made up of a noncompact substance. Which observation suggests the possible presence of cholesterol deposits (inflammatory or not) in front of the drusen (fig. 11).

In the light of the observations of Koelle and Friedenwald,³⁰ this observation is not improbable. They determined that, in the retina, cholesterol activity is greatest at the height of the subjacent, plexiform, internal, granulous layer and bipolar cells.

These observations provide a certain confirmation of the hypothesis herein set forth with the hope that it may contribute some factors to an explanation for a singular ophthalmoscopic condition which is characterized by luminescent crystalline lesions and which has not, to my knowledge, been reported to date in the literature.

Av. Quintana 104.

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ETIOLOGIC CONSIDERATIONS OF VERTICAL MUSCLE DEFECTS*

PART I. GENERAL CONSIDERATIONS: CLASSIFICATION: SUPRANUCLEAR VERTICAL DEFECTS

WALTER H. FINK, M.D.

Minneapolis, Minnesota

The etiology of vertical defects is speculative. I propose to probe into this field, to assemble data concerning the causative factors in vertical muscle defects, and evaluate them on the basis of tangible evidence. Because of the importance of etiology in our concept of vertical imbalance, it is hoped that this discussion may serve to create a somewhat more unified opinion.

Concerning horizontal motor defects much thought has been given and a voluminous literature has accumulated, in which many etiologic factors are more or less accepted. Vertical defects, on the contrary, present a comparatively unexplored field.

A review of available data indicates that our knowledge of the etiology of vertical de-

viations is based largely on supposition. Anderson's findings¹ emphasize this point: in an analysis of 402 cases from an etiologic standpoint he was able to determine the cause of the deviation with certainty in only 10 cases.

That most of our knowledge of the etiology of vertical defects is based on inference is understandable. The horizontal defects lend themselves much more readily to study, both clinically and on the operating table. The vertical defects, because of their complexity, are more difficult to analyze clinically; because of their obscure anatomy, they are more difficult to study at the time of operation; actual knowledge of the anatomy of the vertical mechanism, as revealed in the dissection laboratory, is limited.

The physiology of the vertical mechanism

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is also a matter of controversy. Some maintain it is poorly developed, taking only a passive role in binocular activity, while others consider it a highly developed mechanism, forming the basis of stable binocular action.

We have, therefore, in the vertical defects a problem which is not clearly defined and about which much of our knowledge is speculation. The problem of assembling tangible evidence as to its etiology is therefore difficult and must necessarily be incomplete and open to question.

Nevertheless, study of the etiology of vertical defects is not merely of academic interest; it is of definite clinical value. Knowledge of the etiology of a vertical defect leads to a more accurate diagnosis; successful therapy also demands correct evaluation of the etiologic factors.

An attempt must be made in each individual case to differentiate the static (mechanical) and dynamic (innervational) factors to avoid therapeutic blunders. Surgical treatment can effect a permanent change only in the static (mechanical) conditions; nonsurgical treatment can only indirectly produce a change in the relative position of the eyes. Once proper evaluation has been carried out, therapy rests upon rational and logical grounds. The more accurately we can evaluate the causative factor, the better the ultimate result.

GENERAL CONSIDERATIONS

In order properly to evaluate the various etiologic factors it is essential to consider certain facts concerning vertical motor defects. Not only the manifest error but also the latent ones must be considered.

1. Vertical defects are more frequent than is generally recognized. White and Brown² state that of 1,955 cases of motor anomalies, 36.6 percent of horizontal deviations were complicated by a vertical imbalance. In 402 cases of combined vertical and horizontal imbalance reported by Anderson,¹ 286 showed vertical imbalance.

In Scobee's³ group of 457 patients with esotropia, 195 (43 percent) had paresis of one or more of the vertically acting muscles. The incidence of the vertical component was 49 percent in the nonaccommodative group, 45 percent in the partially accommodative, and 21 percent in the purely accommodative group. (These statistics do not include minor vertical imbalance; if so, the percentage would be appreciably higher.)

2. A vertical defect has certain basic differences in anatomy and physiology which distinguish it from a horizontal defect. Because of this an etiologic factor may assume greater or less significance than the same factor related to a horizontal defect. For example, an accommodative factor due to a refractive error is of greater significance in a horizontal defect than in a vertical defect.

3. One or more etiologic factors may be involved. Some of these are obvious, others are present by inference, still others remain more or less obscure.

4. The etiologic factors present in any given case may vary in importance; some are primary factors in precipitating the defect, others are secondary factors which develop or become manifest as the result of the primary defect. For example, suppose that a superior oblique paralysis is the primary etiologic factor. In its presence an innervational vertical factor may become manifest that would otherwise have remained latent. Or a secondary etiologic factor, such as an accommodative-convergence defect, may become superimposed upon the primary paralysis.

In addition, independent factors may coexist, such as a high refractive error and a paresis. The involved etiologic background is particularly difficult to analyze if the defect has been present for some time.

5. There is a difference of opinion as to the significance of the vertical motor field. Some consider it unimportant, not essential in our daily use, and elementary in its development. Others consider it a highly developed mechanism, by reason of whose great

stability the elastic, adjustable nature of the horizontal field is made possible.

The literature concerning the physiology of the vertical motor field is meager. Very little actual information is available and opinions in this field of oculomotor physiology are based chiefly on supposition. However, it is my contention that the vertical motor mechanism is very important in oculomotor activities, co-ordinated horizontal action being dependent to a considerable degree upon the highly developed physiologic action of the vertical mechanism. That the vertical mechanism is highly developed and that binocular efficiency is dependent upon its stability is evidenced in the study of certain physiologic and anatomic data presented below.

PHYSIOLOGIC DATA

There is some evidence to substantiate the claim that the vertical mechanism is a highly developed stable one, of considerable physiologic importance in binocular activity. In the interests of binocular efficiency, the vertical mechanism must necessarily be a stable one. It is this stability which permits the wide latitude of adaptability of the horizontal motor field fundamental to our daily needs. A disruption of the vertical balance produces a profound change in binocular activities.

1. Physiologic study shows that the vertical mechanism is made up of basic reflexes having certain characteristics of the so-called unconditioned reflexes described by Pavlov.

It is generally believed that all nervous activities are reflex in nature, and may be divided into two classes: the comparatively simple reflex activities of the cord and brain stem, which are structurally determined and transmitted by heredity and are known as unconditioned reflexes; and, superimposed on these, acquired conditioned reflexes mediated by cerebral activity.

The first are characteristic of the species rather than of the individual and occur with extreme regularity, provided the necessary structural basis has developed. The second

each individual acquires for himself out of his own experience; they are being continually created and modified by environmental conditions, cannot be created spontaneously, but can be built up only upon an inborn unconditioned reflex.

Once formed, however, and provided that the neural groundwork is sufficiently plastic, and that continued reinforcement leads to satisfactory reward in achievement, conditioned reflexes can become as firmly established as unconditioned reflexes. The postural reflexes are examples of unconditioned reflexes, innate and automatically complete before birth, functioning independently of ocular stimuli; whereas fusion is a conditioned reflex.

The vertical mechanism displays some characteristics of the unconditioned reflexes. Like the basic reflexes, it is a primitive development in the species and not subject to alteration. This is evidenced by the stability of the vertical mechanism in the newborn.

The newborn possesses the power of conjugating the eyes in vertical movements. The fixation reflex is also innate and present at birth, but it is only feebly developed, responding momentarily to a strong stimulus such as a bright light.

In contrast, the horizontal field exhibits conditioned reflexes. These are acquired, develop after birth, and can be altered by use and training. Horizontal movements are poorly conjugated at birth and require months before becoming stabilized. Indeed, full stabilization usually does not occur for several years, and even then the horizontal movements retain a variability which permits a wide range of flexibility and may, under unfavorable conditions, easily lead to instability. It therefore follows that a defect in the vertical field produces the more profound disruption of forces, of greater significance and presenting a fundamentally different etiologic problem.

2. Physiologic study further confirms that stability of the vertical balance is essential to efficient binocular action. Whereas the ac-

tions of the horizontal muscles are comparatively simple, the co-ordinated actions of the vertical muscles are highly complex, owing to the variable actions dependent upon the direction of gaze.

Because the axes of rotation of the vertical muscles lie outside Listing's plane, vertical movements call for a higher degree of co-ordination, in order that ocular movements may take place around an axis lying in the correct plane.

The action of the vertical muscles must be balanced so that the various components are synchronized. For example, when the eye is turned up or down, the components acting around the vertical and anteroposterior axes are neutralized, leaving those which act around the horizontal axis combined in the correct proportions and thus permitting movement free from unnecessary deviations.

The arrangement of the four vertical muscles represents the most economical way to achieve both vertical movement free of torsion, following Listing's law, and torsion of the eyeball where this is needed. The integration of the various types of muscle action (vertical, horizontal, and torsional), which is present in varying degrees as the gaze is shifted from place to place, necessitates a stable mechanism. Such a stability in the vertical balance gives to the horizontal balance the flexibility essential for accommodation and convergence.

Evidence points to a well-established, highly central mechanism. Clinical and pathologic evidence suggests that the higher control center for vertical ocular motor movements is, for the most part, located in the superior colliculi. Experimental evidence indicates that this area is highly specialized and is closely associated with the reflex centers of the brain. These reflex centers serve to modify the impulses from the superior colliculi.

It is important to note that the vertical mechanism is independent from the horizontal mechanism except for the association in the frontal oculomotor centers where

the willed movements originate.

The separate controlling mechanism for vertical movement, found in the superior colliculi, creates a separate and individualized type of control over the vertical ocular movements which, from a physiologic standpoint, should not be considered as possessing the same influence in binocular activities as found in the horizontal control.

This highly developed central mechanism for vertical movements accounts in great degree for the stability of the vertical balance and the remarkable capacity for adjustments so essential to binocular vision. The co-ordinating mechanism in vertical ocular movements depends not only on gross muscle contractions and relaxations, but also on finely integrated neuromuscular actions (fusional movements) under the control of the higher reflex centers. Such a mechanism must exert a restraining influence, limiting variations in position in order to achieve smooth binocular action in the different fields of gaze.

It is generally agreed that small amounts of vertical imbalance, such as three or four prism diopters, are far more likely to be clinically significant, being associated with definite symptoms, than are equal amounts of either esophoria or exophoria. The reason usually given is that the range of vertical vergence—vertical fusion amplitude—is much smaller than the range of lateral fusion.

The average patient, for example, cannot overcome more than two or three prism diopters of vertical prism without diplopia, and attempts to improve this range are futile. Vertical fusional powers must be very strong in order to accomplish what they do in view of this limited range.

The importance of this stability is further evidenced in clinical work when a vertical muscle is underacting, especially if the superior oblique is involved. The torsional defect coupled with the vertical defect creates a mechanical state which disrupts all other reflex activities and presents a formidable

problem. Lack of proper consideration of the vertical defect has frequently resulted in disappointing therapeutic results.

3. According to Lancaster,⁴ vertical vergence plays a minor role in binocular activity as compared with horizontal vergence. The various binocular adjustments made at different distances call for a minimum effort of the vertical vergence function; vertical movements (up and down) are conjugate, and disjunctive movements are not called for, except to correct minor deviations.

The amplitude of horizontal adjustment is considerably greater. Every change in distance requires a change in horizontal vergence, and therefore a disjunctive adjustment. Horizontal movements are conjugate only when the distance of the fixation is not changed.

ANATOMIC DATA

Anatomic evidence also indicates a highly developed, stable vertical mechanism. Because the eyes are in a common horizontal plane, because of the peculiar anatomic arrangement of the muscles in relation to the globe, the type of insertions, and the specialization of the fascial membranes which produce a check action on the muscles, a high degree of stability is present in the peripheral mechanism. This fact is evidenced by the comparatively small deviation found in the vertical imbalances as compared with the horizontal, also by the small amount of surgical correction required to produce the necessary result.

A study of early embryologic material shows that the anatomic relationship of the vertical muscles is established from the onset. For example, the relation of the obliques to the eyeball is established at the earliest stages and remains in practically the same relation throughout the developmental period. Such an arrangement is evidence of great stability in basic anatomic structure.

Comparative anatomy shows the need for stability and the complexity of the vertical mechanism in man. In the lower vertebrates

the vertical mechanism is less complex and the binocular demands comparatively simple. For example, the obliques predominantly cause a wheel movement, a comparatively simple function. In the bipeds, such as man and monkey, the vertical mechanism becomes more complex. The muscles involved have variable functions, necessary because of the erect position and because the vertical action is associated with lateral and torsional movements. Such actions cause a highly developed integration of forces which can occur only in a highly stable mechanism.

The influence of environment on the development of the vertical mechanism is best illustrated in the case of the superior oblique muscle. Because of its comparative unimportance in our present needs, the inferior oblique continues in a primitive form of development; whereas the superior oblique, because the needs of the biped predominantly require down-and-in vision, is a highly specialized mechanism, in only a limited sense comparable to the inferior oblique.

We have, therefore, in the vertical component a very fixed relationship with very limited range of reflex power of adjustment; in the horizontal component a great power of adjustability. It is only natural that the horizontal balance, which is called on so frequently to make adjustments, should be highly flexible and that the vertical balance, which has very little need for variability in ordinary daily use, should be very stable.

It would seem from the above data that the vertical mechanism has characteristics which are fundamentally different from those of the horizontal mechanism and that a disruption of the normal action of this mechanism would produce situations different in nature from those produced by a disruption of the horizontal mechanism.

Clinical evidence confirms this fact, cases of vertical disturbance showing characteristics which are of diagnostic significance. To cite a few of these changes:

1. Vertical defects are more frequent in early life than horizontal defects.

2. A high percentage of vertical disturbances are due to mechanical defects.

3. Secondary changes such as muscle or fascial contractures are more evident in vertical than in horizontal defects.

4. Because a vertical defect creates a greater mechanical obstacle to binocular action than does a horizontal defect, binocular unity is more difficult to re-establish in the presence of a vertical than of a horizontal defect.

5. There is less tendency for the vertical defect to become concomitant.

6. Fusion training is of little value.

It can thus be seen that an etiologic factor should be evaluated on a different basis when it causes a defect in the vertical mechanism than when a similar factor causes a defect in the horizontal mechanism.

CLASSIFICATION OF VERTICAL DEFECTS

The etiology of vertical defects is too complex to lend itself to accurate classification. When so many factors are controversial, any method of classification is obviously open to criticism, as being too dogmatic or all inclusive. The following classification is admittedly a convenient vehicle for the purpose of presentation.

SUPRANUCLEAR FACTORS

1. Cortical (higher centers and pathways):

Vertical defects attributable to a specific lesion

Vertical defects not attributable to a specific lesion

2. Subcortical (brain-stem centers and pathways):

Vertical defects attributable to a specific lesion

Vertical defects not attributable to a specific lesion

INFRANUCLEAR FACTORS

1. Innervational (motor centers and their peripheral nerves):

Defects of the motor nuclei of the vertical muscle

Defects of the peripheral nerves to the vertical muscles

2. Noninnervational (peripheral mechanism):

Vertical defects related to the eyeball

Vertical defects related to the orbit

Vertical defects related to the fascia

Vertical defects related to the muscles

Statistical studies indicate that inheritance is a factor which must be stressed in the etiology of vertical defects, regardless of whether mechanical or innervational factors are thought to be the more important element in the etiology. Accompanying the ocular deviation in these cases may be various other ocular abnormalities and a general weakness of the central nervous system, a so-called neuropathic condition, manifesting itself in abnormal excitability, combined with abnormal exhaustibility.

Carefully compiled statistics have shown that among the nonsquinting relatives of a squinting child, high ametropia, anisometropia, monocular amblyopia, heterophoria, and weak fusion faculty are to be met with much more frequently than in families which have no squinting member.

SUPRANUCLEAR VERTICAL DEFECTS

For the purpose of presentation, the etiologic factors producing supranuclear vertical defects may be divided into two groups, depending on the level at which the supranuclear system is involved: (1) The cortical centers and pathways where the volitional and reflex movements of the eyes originate; (2) the subcortical centers and pathways which integrate and co-ordinate the cortical impulses and transform them into impulses which stimulate the motor nuclei.

Because of the close interrelation between the two areas it is obviously impossible to make a sharp distinction in the involvement of the two regions. An etiologic factor may be related to both groups although more predominantly to one.

No attempt will be made to discuss all conditions in this highly complicated field, but rather to call attention briefly to a few of the more important factors which serve to illustrate the nature of the processes.

DEFECTS OF CORTICAL VERTICAL OCULOMOTOR CENTERS AND PATHWAYS

Oculomotor defects in this area are usually not seen as isolated phenomena. Cortical defects may be accompanied by disturbances in the subcortical region with symptoms characteristic of disturbances in both regions. Adjacent motor and sensory areas may also be involved, in which case the oculomotor symptoms make up only a part of the clinical picture.

This tendency to a more generalized involvement is due to the anatomic arrangement where there is an intimate relationship and a certain amount of overlapping of the various centers, to the nature of the blood supply and to the effect of increased intracranial pressure.

For the purpose of this presentation cortical oculomotor defects may be divided into two groups: defects attributable to a specific lesion; defects attributable to an abnormal cortical control.

Defects attributable to specific lesion

NATURE OF THE LESIONS. The exact nature of these lesions is frequently unknown, so that opinion in many instances is based largely on supposition. Although in a large number of cases the cortical area seems obviously at fault, such evidence is but occasionally based on pathologic findings. However, although direct evidence is scanty the possibility of the occurrence of such lesions is indicated in the changes found in certain other cerebral conditions in which there is definite pathologic proof.

Developmental anomalies of the oculomotor cortical mechanism occur as in other parts of the central nervous system. Direct evidence as to the existence of such lesions is mostly conjectural, being based on clinical

findings which show a disturbance of the cortical region and on absence of evidence which indicates pathologic lesions such as result from trauma, vascular disease, or tumors.

A developmental defect in this region is usually associated with a similar disturbance in other areas of the cortex. The defect may range from such slight weakness in control as emotional instability or mental retardation to gross anomalies of the cortex which may be associated with other gross anomalies of other parts.

Acquired defects make up the greater percentage of the disturbances found in the cortical area. Acquired cortical disturbances include vascular, inflammatory, degenerative, or neoplastic conditions in the central nervous system and the meninges and trauma of the brain or skull.

It has been estimated that 70 percent of cases of spastic paraplegia in children are due to intracranial hemorrhage at birth, and that 20 percent of all idiots and imbeciles owe their condition to the same cause. The incidence of squint in such cases is very high. If such gross injuries occur with this high frequency, it would seem that injuries minor enough to escape notice at the time, yet sufficient to disturb the balance of the binocular mechanism, must occur with even greater frequency. These often become manifest as an obvious dissociation only at a much later date.

CLINICAL MANIFESTATIONS. *Frontal center for conjugate movements.* The frontal motor area is the principal cortical center for the regulation of the volitional conjugate movements of the ocular muscles. It is situated in the posterior portion of the second and third frontal convolutions, just anterior to the precentral fissure. This center permits voluntary movements of the eyes, because of a command to do so or because of a conscious decision.

Owing to evolutionary transfer of function to higher levels, the frontal cortex has assumed control over other centers and has

the power to neutralize stimuli coming from the occipital and other centers.

Frontal lesions may be either paralytic or irritative in nature. A paralytic lesion involving an oculomotor area is followed by paresis of conjugate gaze to the opposite side, and is always comitant in type. The lesion is a paresis, only rarely a paralysis, of conjugate gaze. The paresis is of movement rather than of individual muscles.

In paralysis, the movements of both eyes past the midline in the direction of paralysis are impossible; the eyes are usually held fixed, turned toward the opposite side by opposing muscles. If the paralysis is only partial, the patient may move both eyes to the other side by willed effort, but fixation cannot be maintained and jerky nystagmus results. The inability to move both eyes is equal, also the degree of nystagmus. The visual axes remain parallel, and there is neither strabismus nor diplopia. There is an increased tonicity of the antagonistic muscles, resulting in a conjugate deviation of the eyes in the opposite direction; this is due to a loss of normal inhibitory influences.

When voluntary control is defective, the fixation reflex is inhibited and the gaze becomes anchored to an object of fixation so firmly that further movement can only be elicited if the reflex is abolished by cutting off all retinal impulses. There is also a retention and intensification of proprioceptive reflexes from the labyrinth and neck muscles. However, they may be overshadowed by the fixation reflex, for if fixation is encouraged during the test, the labyrinthine deviation may be absent, to reappear immediately if fixation is embarrassed by placing a card before the eyes.

The deviation may consist of only a horizontal defect, or it may be combined with a vertical deviation. In the frontal area the vertical component does not appear alone and, as a rule, is of minor degree.

There is some experimental evidence to indicate that conjugate vertical movements are controlled from this area. Most physiolo-

gists now agree that purely upward or downward movements can be produced on stimulation of the oculogyric centers only by (1) first destroying the horizontally acting muscles, (2) stimulating the upper or lower portions of the oculogyric center on both sides simultaneously.

Most of the lesions which occur in the frontopontine pathway produce paresis but, occasionally, instead of interrupting the fibers, the lesion serves merely to irritate them; instead of being weakened the fibers are stimulated and the muscles concerned are sent into spasm.

Paresis of an oculomotor cortical area is, as a rule, transient; recovery follows rapidly because the function of the damaged cortex is taken over by the other hemisphere. If the lesion is bilateral, the defect may be permanent.

Irritative lesions involving the frontal oculomotor centers produce conjugate deviation of the eyes away from the irritated side. As a rule, the adjacent motor center is also irritated and the head is turned in the same direction as the eyes; in the usual more extensive lesions, both head and eyes are turned in the direction of the convulsed limbs. In contradistinction to paretic lesions, conjugate spasm is more commonly cortical than subcortical.

Irritation of the oculomotor center in the cortex produces lateral deviations with great regularity, but only exceptionally have vertical deviations been noted. If the lower portion of this area is irritated, the eyes are deviated upward and laterally; if the upper portion is irritated, they are moved downward and laterally. There may be associated opening of the eyelids and dilatation of the pupils.

Conjugate deviation of the eyes of a spasmodic nature may occur in association with a paralysis of movement in the opposite direction due to a unilateral cortical lesion. In this case the deviation is due to uninhibited activity of the undamaged hemisphere. In cases of pure conjugate deviation in one di-

rection, movement in other directions is possible unless the spasm is excessive. These cases are due to an irritative lesion in the oculomotor centers or tract. In a progressive lesion, an irritative type of deviation may be followed by a paretic type; a spastic deviation to one side is then replaced at a later stage by a paretic phase, and the eyes are deviated to the other side.

The oculomotor symptoms usually constitute but a portion of the over-all picture; for example, in trauma of the frontal cortex the oculomotor deviation is accompanied by other findings such as choked disc, nystagmus, and headache. Frequently mental changes are presented, characterized by loss of memory for recent events and either a depression or euphoria. Facial weakness of central type, on the opposite side of the lesion, has been stressed as a frequent sign. Hemiparesis on the side opposite the lesion is commonly present. Signs of pituitary or infundibular involvement are not common.

In vascular accidents involving this region there is also a close association between the oculomotor disturbance and disturbances of other areas. This is especially true of other motor areas, so that the clinical picture may include not only an oculomotor defect but a widespread motor disturbance. Such association between the oculomotor disturbance and disturbances in adjacent areas is seen in other types of cortical involvement such as result from tumor, brain abscess, meningitis, and so forth.

Occipital center for conjugate movements. Conjugate movements of the eyes may be produced not only by stimulation of the frontal oculomotor center, but also by stimulation of a center in the occipital lobe. The frontal center has to do with voluntary and conscious stimuli, whereas the occipital center has to do with response to visual stimuli.

The occipital center is a reflex rather than a volitional center, and is important in maintaining visual attention. The frontal oculomotor area opposes and dominates the occipital oculomotor center.

If lesions of the frontal area involve paresis of voluntary movements, the occipital reflexes become uninhibited and uncontrolled, resulting in occipital dominance. Therefore, in contrasting occipital with frontal lesions, the outstanding difference is in ocular fixation.

The occipital zone corresponding to fields 17, 18, and 19 of Brodmann, especially field 19, is the cortical center for optically induced eye movements and optic fixation reflexes.

Stimulation of this center in man produces deviation of the eyes to the opposite side and visual hallucinations. As in the frontal lobe, the visual areas in the occipital lobe have portions concerned in vertical movements. Like those in the frontal cortex, these are intimately associated with lateral movements.

Stimulation of the most dorsal portion of field 19 results in upward conjugate deviation of the eyes; stimulation of the lower area causes downward conjugate movement. Fibers from this area have been traced to the superior colliculi and from here to the oculomotor nuclei.

The movements of the eyes obtained by stimulation of the occipital cortex are slower, weaker, and less constant than those obtained from frontal lobe stimulation.

In destruction of occipital visual cortex all the purely optical reflexes are lost; the only motor reflexes remaining to the eyes are the pupillomotor and voluntary convergence. There are thus no fixation reflexes, no fusion movements, no protective visual blinking reflexes, neither involuntary convergence nor accommodation.

Fixation disturbances are usually the most prominent; when asked to look at anything, the patient stares straight ahead or in the direction in which he has previously been looking, or rolls his eyes about. In bilateral lesions the inability to maintain fixation is complete; in unilateral cases the symptoms are less pronounced, but there may be difficulty in maintaining fixation, especially if the gaze is directed to the side. There is an

inability to keep the eyes steady in a position to which they have been brought voluntarily. In other words a voluntary movement is possible, but it is not supported and maintained by the fixation reflex.

Stimulation or irritation of this region of the cortex has been observed to give rise to conjugate deviation, but few clinical signs of spastic deviation have been reported from lesions in this area.

As in the case of the frontal oculomotor cortex, the oculomotor symptoms are but part of the clinical picture, and are accompanied with other evidence of occipital involvement. There may be a disturbance of the calcarine cortex (area 17) producing unformed visual hallucinations, such as scotomas and flashes of light, in the corresponding fields of vision. Destructive lesions result in defects in the visual fields corresponding to the affected areas. Bilateral destruction of this region causes total blindness.

There may be disorientation of the psych-optical reflexes which originate in areas 18 and 19. Areas 18 and 19 receive and interpret impulses from the calcarine area 17, and, when stimulated, formed visual hallucinations result. Destruction of areas 18 and 19 is followed by difficulty with accurate localization and discernment of objects and by disturbances in the spatial orientation of the visual image in the homonymous field. There may be loss of ability to discriminate with respect to size, shape, and color. Epileptiform attacks, frequently an outstanding symptom, occur in slightly more than half of the cases. Headache, the commonest symptom, is not localized.

Lesions involving the occipital oculomotor mechanism are not so common as those affecting the frontal. This difference in occurrence may be only apparent, however. There is more difficulty in recognizing anomalies in ocular movements due to occipital lesions because they are commonly associated with defective vision and hemianopia.

Temporal center for conjugate movements. Lesions of the temporal lobe also

cause conjugate deviations but are dominated by the frontal oculomotor area, and to a less extent by the occipital area. As in the case of the other areas, the lesions may be paretic or spastic in nature and take on many of the characteristics previously described.

They are not voluntary in nature, but rather reflex, as in the occipital area. Also they are intimately associated with and dependent upon reflex action, such as the auditory impulses.

As in the case of the other areas, the oculomotor symptoms make up but a part of the clinical picture. For example, in tumor of the temporal lobe, the conjugate deviation is accompanied by such findings as convulsions. Indeed these occur with greater frequency in temporal lobe tumors than in any other cortical tumor. Aphasia is an early sign of tumor of the temporal lobe. Loss of hearing and disturbed vestibular functions are also prominent symptoms. Papilledema is usually present in both eyes, but may be entirely absent.

Vascular lesions may also cause a variety of symptoms and signs. Symptoms resulting from occlusion or rupture of a cerebral artery in this area include hemiplegia, hemianesthesia, hemianopia, receptive aphasia with alexia predominating, and other associated symptoms. Involvement of certain portions of the temporal lobe, especially the anterior, causes disordered consciousness, with possible auditory and visual hallucinations.

Defects attributable to abnormal cortical control

In this group the clinical manifestations cannot be attributed to a specific etiologic factor, such as tumor or trauma; the association is rather with mental processes about the physiology of which we have little knowledge. Such conditions do not act as a primary etiologic factor in producing a vertical defect but rather as a precipitating or an adjunctive factor in the presence of some more disturbing cause.

DEVIATIONS DUE TO NERVOUS INSTABIL-

ITY. Some cases of strabismus are associated with nervous instability. They may be unassociated with any apparent physical factor (such as a high refractive error). In these cases, the general make-up of the individual (as in feeble-mindedness) may not be competent to undertake the complex task necessary for the attainment of binocular vision.

PHYSIOLOGIC SQUINTS. After the establishment of binocular reflexes a lowering of cerebral efficiency may lead to their breakdown. Any strong emotion, physical shock, or physical or mental illness is apt to disturb the power of maintaining binocular processes. In such squint the central influence is therefore not the sole cause of the condition but a determining and adjuvant factor, acting only in the presence of anatomic or innervational imbalance.

PURPOSIVE SQUINT. Here a marked disparity exists between the two retinal images. Their simultaneous projection into consciousness may not be tolerated, with a resulting condition called horror fusionis. Relief is sought by suppressing one image and one eye deviates if any tendency toward squint exists.

DEFECTS OF SUBCORTICAL VERTICAL CENTERS AND PATHWAYS

For the purpose of presentation, defects of the subcortical region may be divided into two groups: defects due to a localized lesion, defects in which a localized lesion is not evident.

Defects due to a localized lesion

NATURE OF SUBCORTICAL VERTICAL LESIONS. The etiology of subcortical oculomotor lesions has caused considerable controversy. An analysis of these cases shows that only in some is a recognizable factor present; in the great majority the lesion is speculative and hypothetical lesions are attributed to structures whose normal functions are not clear.

Many observers believe that certain localized regions or centers exist in the sub-

cortical area. Even in the face of insufficient evidence, it is, in many instances, necessary to assume their existence to account for the change in character of the cerebral and postural impulses which stimulate the oculomotor nuclei. Spiller (1924), however, contends that the phenomena can be equally well explained by a simple reshuffling of nerve fibers in their course down the brain-stem.

The descending pathways carrying impulses for vertical movements of the eyes from the frontal cortex to the lower centers have not been identified histologically, but their course is probably somewhat as follows:

Having passed through the internal capsule, the fibers for vertical gaze divide from those for horizontal gaze. While most of the fibers for horizontal movements pass downward to the pons, most of the fibers for vertical movements are believed to travel to the superior colliculi. This course is inferred from the fact that lesions of the pons produce disturbances predominantly of the lateral movements, whereas lesions of the superior colliculi produce disturbances predominantly of the vertical movements.

The descending pathways carrying impulses from the occipital cortex for vertical movements of the eyes pass through the optic radiations in the posterior limb of the internal capsule to the superior colliculus and the tectum of the midbrain, and then through the medial longitudinal fasciculus to the nuclei of the ocular nerves. Through this latter pathway the fibers have connections with the vestibular nuclei, the accessory nuclei, and the nuclear centers in the upper portion of the spinal cord.

Abnormal innervations acting upon these centers, caused by unbalanced reflex influences or by the removal of normal inhibitory controls, may be responsible for the development or the continuance of ocular motor deviations.

The cause of the lesion may be developmental or acquired. The developmental lesions vary with the type and degree of ab-

normal development, depending upon whether the fixation reflexes or the conditioned reflexes are involved and the degree of involvement.

If there is bilateral failure in the development of fixation, the defect tends to produce nystagmus, but if the fixation is established and there is a disturbance in the development of conditioned reflexes, concomitant deviation is present (provided the motor apparatus is intact and the eyes are yoked together by the postural reflexes). Abnormal impulses or instability of the mechanism, as seen in the dissociated type of defect, may be attributed to a lack of stability or maturation of the mechanism in the absence of an obvious etiologic factor such as trauma, vascular disease, or tumors.

The acquired lesions are usually due to trauma or a space-taking lesion, such as tumors or abscess. Vascular lesions are also relatively frequent; encephalitis, disseminated sclerosis, syphilis, and other conditions may also be responsible.

CLINICAL MANIFESTATIONS OF LOCALIZED SUBCORTICAL VERTICAL LESIONS. In paretic lesions of this area, deviation of the eyes is not so great as in the cortical lesions but is more enduring.

The lesion may affect either lateral or vertical conjugate movements. In lateral movements, a destructive lesion causes paresis of conjugate movements to the opposite side, if it is located above the decussation of the corticonuclear tract in the midbrain, and to the same side if in the pons below the decussation. If the lesion is bilateral, so that lateral movements are abolished, vertical movements may be retained.

In subcortical lesions certain types of movements are affected. If the command movements, the following movements, and the attraction movements are absent, the lesion is probably somewhere near the pons. If the vestibular impulses are also absent, the lesion is in the pons and probably also affects the nuclei.

Torsional conjugate mechanism should be considered in subcortical involvement. Conjugate torsional movements are produced by appropriate vestibular and postural stimuli and are evidence of their association with the vestibular mechanism.

Rotary nystagmus is seen in lesions of the vestibular nuclei in the floor of the fourth ventricle and is associated with such conditions as multiple sclerosis. Aside from rotary nystagmus, disturbances of the conjugate torsional mechanism are apparently very rare, although they are manifest in a superior oblique paralysis of one eye, when head tilting is used to produce a similar position of the other eye and thereby to avoid diplopia.

Judging from the meager clinical evidence available, there is probably some torsional representation in the occipital lobe, because torsional following movements can be induced by rotation of the field of vision.

From a clinical standpoint the subcortical structures of special interest are the superior colliculi, the medial longitudinal fasciculus, and the pons.

The superior colliculi is an important center in relation to vertical movements. It is a relay station in the pathway for vertical movements of the eyes, similar to the pontile center for lateral gaze. In man it occupies a subordinate role, being dependent on impulses from the cortex.

Evidence indicates that the region of the superior colliculi contains association centers which serve to co-ordinate vertical conjugate movement. A lesion of the anterior end causes loss of upward movement. A lesion more posteriorly situated accounts for loss of conjugate downward movement; and a lesion still more posterior is said to affect convergence.

Localized damage causing loss of vertical movements most usually affects upward movements, less frequently both upward and downward movements, and least frequently downward movements alone. Paralysis of upward movement or of all vertical movements

may be combined with paralysis of lateral movements. A further variation is the combination of a loss of vertical movements with paralysis of convergence and reflex pupillary disturbances.

If the paralysis is upward and not complete, the eyes may be moved slightly above the midline, showing upward vertical nystagmus. In paralysis of downward gaze a similar picture is present except for the direction of limitation of movement.

The condition might be confused with a disturbance of both superior recti and inferior obliques which is due to involvement of the motor nuclei of the third nerve. If Bell's phenomenon is present in cases showing a disturbance of upward gaze, it proves that the nuclei of the superior recti and of the inferior obliques are intact, and that the lesion must be supranuclear.

Lesions of the superior colliculi or its immediate vicinity are relatively common and are the most frequent cause of conjugate palsies of the vertical gaze. Paralysis occurs as the result of tumors, hemorrhage, and inflammatory processes. Tumor of the pineal gland is an especially common cause.

Paralysis of vertical movements occurs with lesions of other structures beside the superior colliculi. Vertical palsies, vertical nystagmus, and spasms of vertical gaze also occur with lesions of the fourth ventricle and cerebellum. However, the signs produced by these lesions differ from those occurring with lesions of the colliculi in the retention of normal pupillary reactions and, usually, the presence of nystagmus.

There is reason to believe that some regulation of vertical movements occurs in the medulla and possibly in the vestibular nuclei. Not only is vertical nystagmus frequent with lesions in this region, but vertical movements of the eyes may be induced by labyrinthine stimulation in patients who, on account of lesions of the tectum, cannot otherwise move their eyes vertically.

It is impossible to be dogmatic about the

exact location of all the fibers for vertical gaze in man because of the complexity of the mechanism and a lack of adequate anatomic and physiologic data.

The *medial longitudinal fasciculus* is the important connecting mechanism in the co-ordination of impulses reaching the nuclei of the oculomotor nerves. It transmits impulses determining volitional movements from the frontal oculomotor centers and from the occipital centers which control ocular fixation; through its connection with the auditory apparatus it determines movements of the eyes which are dependent upon stimuli from the vestibular and cochlear nuclei; from the sensory nucleus of the fifth nerve, the cerebellum, the spinal medulla, and the muscles of the neck it likewise conveys stimuli which influence the position of the eyes. Owing to the function of this correlating mechanism, no isolated action of any eye muscle is ever possible.

Lesions of this area prevent co-ordination of the various cortical and subcortical impulses. They may also affect the pathways by which the various ocular nuclei are linked together; when this occurs, conjugate movements may be disrupted.

These lesions may have a vascular origin but are usually seen in multiple sclerosis and encephalitis lethargica.

As to the *pons*, although there is no histologic evidence for its existence, the majority of authors believe that the fibers from the higher centers end in a pontile center. This so-called pontile center receives all the stimuli which produce horizontal conjugate movements of the eyes, including voluntary movements, reflex horizontal movements from the lower visual and auditory systems, proprioceptive impulses from the neck muscles, and impulses from the visuomotor center in the occipital cortex.

In pontine lesions the deviation is of small magnitude but is usually permanent. Pontine lesions are usually parietic rather than irritative. In parietic pontine lesions (below

the point where the corticobulbar fibers cross the midline to reach the opposite side of the pons), there is paresis of gaze toward the side of the lesion, with deviation of the eyes toward the opposite side.

Paresis of the associated muscles may be asymmetrical, and there may be associated nuclear palsies. There may be paresis of conjugate gaze, with retention of convergence. There may be lessening of ability to turn the eyes laterally on command (volitional control), but reflex lateral movements in response to visual, vestibular, and acoustic stimuli, and in response to turning movements of the head and body, may be retained.

When the lesion is in the part of the pathway near the pons, the diagnosis is more difficult, because some of the reflex fibers may be caught in the lesion. In general, the farther the lesion from the ocular motor nuclei, the easier the diagnosis.

The deviation is rarely an irritative symptom. In the upper part of the pons the clinical aspects of an irritative lesion are identical with characteristics of cortical lesions; but in the middle part of the pons, where the decussation of the oculomotor fibers leads to a different distribution of spasmodic effects, there is ocular spasm to the same side as the lesion, with spasms of the face and extremities to the opposite side.

Pontine lesions are usually due to hemorrhage or tumor. When due to intrapontine hemorrhage, symptoms tend to be complete at the time of first examination. With tumor of the pons the symptoms are likely to be progressive and an early defect in conjugate movement can easily be overlooked. As time passes, supranuclear and nuclear paralyses are added.

Defects of the subcortical area in which a localized lesion is not evident

CONVERGENCE DEFECTS (nonaccommodative). The etiologic factor in convergence abnormalities is of interest in the consideration of vertical defects because of their fre-

quent association with horizontal defects. It is possible that an abnormal convergence mechanism could be a primary etiologic factor in a horizontal defect and an associated etiologic consideration in a vertical defect; or perhaps a less common precipitating primary cause of a vertical imbalance.

Characteristic of these abnormal convergence innervations is the variability of the angle of squint, depending on the general physical and psychic condition of the patient.

The origin of the abnormal convergence (nonaccommodative) impulses is not known. It has been suggested that they are due to the loss of normal supranuclear control of the convergence mechanism.

Bielschowsky⁵ considered the seat of the lesion to be subcortical, because the fluctuating tonic convergence innervation is not accompanied by corresponding fluctuation in accommodation and pupillary size, as would follow if the convergence impulses originated in cortical centers (for example, in hysterical spasms of convergence).

A review of the supranuclear pathways for the eye movements led Adler⁶ to conclude that the seat of the disturbance is likely to be in the subcortical centers and pathways for convergence and divergence. Adler points out that there is no evidence that other structures are involved; even for the subcortical centers and pathways for convergence and divergence the evidence is merely suggestive. Such evidence is mainly based on analogy with the conditions of acute alcohol intoxication and severe anoxia in which the visual axes allegedly become convergent.

Adler⁶ states, "In all cases of convergent squint, except those in which the condition is due to paralysis of an ocular muscle, the fundamental cause is an abnormal convergence innervation." He further states, "Regardless of the state of perfection of fusion, the important factor in the causation of squint is the force which produces it, and that it is an excessive convergence innervation."

Adler's innervational theory has the advantage of providing a single explanation for all cases of concomitant esotropia, but it does not conform to some clinical experiences. As Burian⁷ points out, "One should hardly expect the angle of squint for distance to be as stable as it is in most cases if it were entirely the result of an innervational disorder, and the results of operative treatment would not be as good as they are if the necessarily variable innervational disorder were the sole cause of strabismus."

It is evident that such explanations have little basis. However, clinical and pathologic data indicate that a paralysis of convergence occurs following such lesions as encephalitis, disseminated sclerosis, syphilis, hemorrhage, acute infections, trauma, and tumors in the subcortical region.

The exact location of the center for convergence is not known, but some evidence seems to indicate that paralysis of convergence results from a lesion affecting an infracortical area near the superior colliculi. However, convergence paralysis is rarely an isolated symptom but is frequently combined with other lesions denoting more widespread damage in the neighboring region of the brain-stem.

Such evidence therefore suggests a center for convergence, and it is conceivable that if such a center does exist, it can be influenced by abnormal excitations and account for the nonaccommodative type of convergence defect. Such abnormal convergence impulses may be due either to lack of maturation of the controlling center or to interference with the conditioned reflexes while in the process of developing.

Fusional defects. Defects of the fusion mechanism are a supranuclear etiologic factor of importance in binocular activities. They are of major importance in the horizontal defects, exerting a powerful controlling influence over this very adaptable mechanism. In vertical defects, because of the stable nature of the vertical mechanism, fusion defects are of less significance. How-

ever, they do play a significant role as a precipitating factor in the presence of a primary etiologic factor such as a mechanical defect.

The fusion mechanism is a well-recognized entity, even though it has never been located anatomically. A defect of the fusion faculty can be shown only by inference. It is commonly believed that the fusion process is not confined to the subcortical region but involves the entire supranuclear mechanism. It is discussed under the subcortical heading because it is believed by many that the subcortical region is where the conditioned reflexes are chiefly located.

An innate lack of fusion is believed very rare. Absence or defect is due to an interference with the normal state of the conditioned reflexes. Such abnormality may result from a disturbance in the normal development of the conditioned reflexes, or from a disturbance in normally developed reflexes, such as results from infranuclear obstacles or supranuclear disturbances seen in pathologic processes. Low-grade mental capacity, as in imbeciles, is closely related to the development of fusion.

The fusion mechanism is very adaptable. Its capacity of compensating for any interference explains its ability to overcome the mechanical defects created by moderate anatomic variations in the attachments of the muscles or the structural details of the orbit. The capacity for caring for such handicaps is a variable factor, depending upon specific development in the individual. Adjustment ability can be altered by various situations, causing the fusion mechanism to be weakened to the point where it cannot compensate for mechanical or innervational defects.

Vertical deviations of dissociated type (alternating sursumduction). The cause of this condition is unknown, but it is said to be brought about by excitations of the centers of vertical divergence. Although difficult to classify, these deviations may be discussed under this category.

They are generally associated with other nervous factors unrelated to the eyes, and are present in cases with poor fusion as well as in cases with high degrees of strabismus. They are a complication of the typical concomitant as well as the typical parietic motor anomalies of the eyes.

According to Bielschowsky, the vertical deviation is due to intermittent excitation of the vertical divergence centers. He was not in accord with Duane and others, according to whom this anomaly is based on a muscular imbalance between the elevators and depressors, the elevators being stronger. Bielschowsky said this cannot be reconciled with the fact that the upward deviation of the covered eye is inconstant and may become a deviation of the opposite kind.

Vertical dissociation with unilateral amblyopia. This condition is related to the deviation of dissociated type. Not uncommonly, while a good eye maintains fixation of a light, its visually defective fellow will show a series of irregular vertical movements. These can be arrested and replaced by a downward rotation if a dark glass is put before the fixing eye.

Periodical vertical squint. In this condition one eye turns up or out when the patient is fatigued or diverted, returning to normal fixation when an object attracts the attention of the other eye. Lack of fusion power is a factor in this condition. Undoubtedly other factors such as mechanical defects may be contributory causes.

There may be controlling spheres for uniocular and binocular vertical movements not necessarily well defined structurally but ade-

quate under certain conditions to permit unilateral movements.

Pseudoparetic hyperphoria. This is a primary overfunction of one or both inferior obliques; in these cases no parietic element is evident. There is no deviation in the primary position, nor any increase in looking up or down; only on horizontal movements of the eyes is there a tendency for the adducting eye to shoot upward and inward instead of remaining on the horizontal plane. As a rule, the deviation becomes a frank hypertropia.

This resembles the picture produced by paralysis of both superior obliques or paralysis of both superior recti, with secondary contractures of the inferior obliques. It may be distinguished from such paralysis by the fact that there is slight or no hypertropia in the primary position, although hyperphoria may be present. Furthermore, in pseudoparetic hyperphoria the deviation does not increase or decrease upon looking up or down, but is seen only in the lateral movements of the eyes.

Although various theories have been advanced to explain this phenomenon none of them seems to be conclusive. Certain authors attribute it to an innervational disturbance of the subcortical area. For example, Guibor* concluded that excessive accommodative convergence impulses irradiate to the nucleus of the inferior oblique muscle, causing what he termed a synkinetic overfunction of that muscle. It is not clear why this irradiation should be selective.

Medical Arts Building.

(To be concluded)

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AMBLYOPIA IN ADULTS*

TREATMENT OF THOSE ENGAGED IN THE VARIOUS INDUSTRIES

M. D. KASSER, M.D., AND J. B. FELDMAN, M.D.
Philadelphia, Pennsylvania

SURVEY OF PRIVATE PATIENTS

During the last seven-year period, two percent of all patients seen at the eye clinic of the Medical Center of Philadelphia were amblyopic. Since these patients are adults and the majority are of presbyopic age, recognized treatment for this condition—use of atropine, covering the good eye, and so forth—is impractical and cannot be used.

We have, however, been employing eye

It was found, however, that adults were less co-operative than had been expected and that children were more regular in attendance. In view of this, when the idea of visual training was suggested to amblyopes at the clinic and these adults were eager to begin this form of eye training, it was felt that a study of all adult amblyopes previously treated by us as private patients, would be interesting.

TABLE 1

ADULT AMBLYOPIC PATIENTS WHO GAVE GOOD PROGNOSIS ON THE TELESCOPIC AMBLYSCOPE

Case No.	Patient	Sex	Age (years)	Initial Visual Efficiency (percent)	Number of Lessons	Final Visual Efficiency (percent)
1	B. B.	F	36	76.5	5	91.5
2	Y. B.	F	32	76.5	6	91.0
3	D. C.	F	35	83.6	3	91.5
4	H. F.	M	32	87.5	3	93.0
5	A. H.	M	37	66.0	12	90.0
6	H. M.	M	35	77.0	7	91.5
7	H. L.	M	37	64.0	12	96.0
8	C. M.	M	25	83.6	12	97.0
9	R. S.	F	40	64.0	5	91.0
10	J. S.	M	35	83.6	3	91.5
11	J. S.	M	31	89.0	36	94.0
12	H. B.	M	60	76.5	4	64.0
13	D. C.	F	45	76.5	5	69.0
14	M. L.	F	35	76.5	12	83.6
15	S. R.	F	45	64.0	12	80.0

training† in adult patients, just as in young patients, for about 10 years.¹⁻⁴ In 95 percent of selected cases of amblyopia in both hospital and private patients, the results have been successful. Adults were screened with the telescopic amblyoscope and 12 weekly lessons were given, followed by a month's rest period to determine the stability of the visual correction.

* This work was sponsored by the Medical Center of Philadelphia, International Ladies Garment Workers Union.

† An amblyopic eye obtaining 6/6 vision with the telescopic amblyoscope will with training eventually obtain normal vision.

Table 1 reviews a group of amblyopic patients who obtained visual training on the telescopic amblyoscope. All gave good prognosis on the device. Some took as few as three lessons. With the exception of Cases 12 and 13, the vision of every patient in this group improved. None, however, obtained 6/6 vision. Only five patients (one third) completed the first series of lessons and, in spite of improvement, not one returned to obtain 6/6 vision. Only one patient took three series of lessons.

It is interesting to note that the speed of improvement in vision varies with each individual. Thus Cases 1, 2, 12, 13, and 14 each

TABLE 2
ADULTS WHO REQUESTED EYE TRAINING IN SPITE OF POOR PROGNOSIS

Case No.	Patient	Sex	Age (years)	Initial Visual Efficiency (percent)	Number of Lessons	Final Visual Efficiency (percent)
1	J. A.	M	40	20.0	8	64.0
2	M. B.	F	42	20.0	8	20.0
3	R. D.	M	34	11.7	58	48.9
4	I. G.	M	29	48.9	3	62.0
5	J. K.	M	25	48.9	12	85.0
6	A. O.	F	43	83.6	4	83.6
7	M. P.	F	44	80.0	3	83.6
8	R. P.	F	46	20.0	16	58.5
9	L. R.	F	57	48.9	5	64.0
10	S. Z.	F	39	69.9	2	74.0

began visual training with 76.5 percent initial visual efficiency, yet each gave varying results. Cases 7 and 15 began with the same percentage of visual efficiency and each took 12 lessons but obtained different results. The same number of lessons were taken by Case 14 and Case 15; the percentage of final visual efficiency was different. All of which shows that the rate of progress in similar cases varies with the same type of training.

Occasionally, the vision will retrogress, as was observed after several lessons in Cases 12 and 13. From our experience this does not necessarily mean that the patient is getting worse. Quite often after this recession in vision, there will be observed a marked improvement. With adults, however, a temporary visual recession reduced early enthusiasm for treatment—"the cure did not seem to come fast enough."

Except for Case 11, a few patients discontinued treatment after taking as few as two or three lessons. Even the five (one third) patients who took 12 lessons never returned for a recheck of their vision, as was advised.

The adults surveyed in Table 2 asked for and were given eye training even though, when examined with the telescopic amblyoscope, they were told that the prognosis was questionable.

We accepted these cases for two reasons:

1. To see if the prognosis (on the telescopic amblyoscope) was as valid for adults as for the child.

2. We wanted to learn how long the enthusiasm of these patients would last.

Three of the patients took 12 or more lessons; about the same number took only three lessons or less, in spite of their initial enthusiasm.

Only one patient, Case 2, showed absolutely no improvement. The remaining patients varied in increasing their visual efficiency. Only one patient (Case 3) who had very little vision was persistent in his treatment. He had 58 lessons and improved his visual efficiency from about 12 to 49 percent. Knowing that the prognosis was poor, however, we thought his treatments should be discontinued.

TABLE 3
NYSTAGMIC PATIENTS GIVEN TREATMENT IN SPITE OF POOR PROGNOSIS

Case No.	Patient	Sex	Age (years)	Initial Visual Efficiency (percent)	Number of Lessons	Final Visual Efficiency (percent)
1	A. L.	M	37	O.U. 58.5	42	69.9
2	L. M.	M	26	O.U. 64.0	22	76.5
3	E. R.	M	25	R. 64.0 L. 48.9	6	69.9 48.9

TABLE 4
MEDICAL CENTER PATIENTS WITH GOOD PROGNOSIS

Case No.	Name	Sex	Age (years)	Initial Visual Efficiency (percent)	Number of Lessons	Final Visual Efficiency (percent)
1	L. S.	M	39	83.6	12	90.5
2	A. M.	F	47	76.5	12	97.0
2	M. R.	F	56	76.5	12	91.5
4	Y. W.	F	35	64.0	12	93.5

NYSTAGMIC PATIENTS

Three patients with nystagmus are shown in Table 3.

While it was not expected that visual training would correct this congenital condition of central origin, still it had been observed that vision may improve and often the movements of the eye do appear to slow up somewhat.

For example, Richard E., aged 12 years, was treated by us. He had rotary nystagmus and a refraction of: O.D., 1.0D. sph. \ominus 3.0D. cyl. ax. 90° ; O.S., 2.0D. sph. \ominus 2.0D. cyl. ax. 90° . His original corrected vision was 6/15 in both eyes. His final vision, after training was: O.D., 6/9; O.S., 6/6-4. He has retained this vision for about a year, being tested on different types of reading charts. His teachers have voluntarily reported his scholastic improvement.

The vision of the first two patients improved. E. R. (Case 3), who had rotary nystagmus with anisometropia in the left eye, showed no improvement after the sixth lesson.

The reason for including this group in the report was to show that even some nystagmic eyes will recover some amblyopic visual loss with training. Since this is so, it would seem that a nonmoving eye should be even more amenable to visual training.

It should be mentioned here that the visual fields for white, red, green, and blue produced no significant results except for an occasional central scotoma with a minute white target. Nor did examination by pure monochromatic ophthalmoscopy give a retinal picture pathognomonic for amblyopia.

AMBLYOPES AT THE MEDICAL CENTER

It was felt that the problem would be different with the patients at the Medical Center. Amblyopia is most important to these patients. They are either self-supporting or have someone for whom they are responsible financially and can see how important an accident to the only eye with good vision would be. Such persons could be expected to be very co-operative. The way in which these patients had enthusiastically accepted our advice about training made us feel that they would come regularly for training.

The workers at the Center are older, more intelligent, and possess greater powers of concentration than the children whom we usually train. For this reason and for economic reasons, we felt that it was not necessary to have a college-trained technician but rather an intelligent person sympathetic to the problem and trained under our guidance for this position.*

To date six cases have been selected for training, four with good prognosis and two patients with poor prognosis to serve as controls. A further report will be given when a suitable number of cases have been treated.

From the beginning of treatment, it was observed that the Medical Center patients were more enthusiastic and showed better results than the group of private patients. They attended regularly, even though they lost one-half day or more of their pay on the lesson date. Table 4 surveys the four pa-

*We are indebted to Miss Leona Rufus for fields, synoptophore studies, and so forth, and to Miss M. Herstein of the Medical Center for her co-operation.

TABLE 5
MEDICAL CENTER PATIENTS WITH POOR PROGNOSIS WHO SERVED AS CONTROLS

Case No.	Name	Sex	Age (years)	Initial Visual Efficiency (percent)	Number of Lessons	Final Visual Efficiency (percent)
5	L. B.	M	46	64.0	4	87.5
6	D. W.	M	56	20.0	6	64.0

tients with good prognosis and Table 5 the two patients with poor prognosis who, for the initial study at the Medical Center, were used as controls. In each case, the control patients were dropped because, after a few lessons, the reading on the telescopic amblyoscope still gave a poor prognosis, despite the improvement in vision.

SUMMARY AND CONCLUSION

Amblyopia is a condition wherein the patient sees poorly without any apparent pathologic condition of the eye. It is due to a number of causes; sometimes the cause is unknown.

An instrument called the telescopic amblyoscope is used for treatment, as well as to determine the prognosis. This device has proven very successful in treating children if they are treated early before other eye complications develop. In adults, despite their

better powers of concentration, results of treatment with the telescopic amblyoscope have been somewhat less successful because of irregularity in attendance and a tendency to stop treatment as soon as some improvement is noted.

At the Medical Center, the problem is different. These adults, who work for a living and know how important their sight is, gladly sacrifice one-half day's work or more for visual training. This in itself should bring better co-operation and results. In the main even such stubborn cases as those of nystagmus, which have a poor prognosis, show some improvement with eye training.

This is a preliminary paper on amblyopia of adults. When a more exhaustive survey is completed, the total results will be given in a final paper.

37 South 20th Street (3).

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OPHTHALMIC MINIATURE

I recognize three varieties of myopia:

1. The myopia of an eye perfectly healthy.
2. Functional myopia, due to spasm of the accommodation.
3. Myopia, symptomatic of a disease of the eye, of choroiditis.

E. Landolt,

Ophthalmic Hospital Reports, 9:345, 1879.

NOTES, CASES, INSTRUMENTS

CORRELATION OF INTRAOCULAR PRESSURES*

WITH MICROSCOPIC SECTIONS FOLLOWING
CYCLODIATHERMY ON NORMAL RABBITS

J. ALEXANDER VAN HEUVEN, M.D.

AND

JAMES PHILIP DUNN, B.A.

New Haven, Connecticut

This study was undertaken in an attempt to correlate findings on histologic sections and intraocular pressures following cyclo-diathermy on normal rabbits. The nontreated eyes served as controls.

PROCEDURE

After establishing a baseline of intraocular pressure using a Schiötz tonometer, each animal was subjected to cyclo-diathermy over one half of the eye at a distance of three mm. from the limbus using a two-mm. non-perforating electrode. The end-point was considered to be at the time the sclera assumed a parchment appearance.

Tension readings were taken immediately postoperatively, four hours and eight hours later, and then twice daily until the animals were killed—one, three, six, and nine days after operation. Both eyes were removed and sectioned in paraffin.

RESULTS

The postoperative intraocular pressures showed an immediate and severe rise to levels from 59 to 70 mm. Hg, decreasing rapidly, however, so that four hours postoperatively all eyes were hypotonic.

This fall continued more slowly over the next 24 hours reaching levels which could not be read on the tonometer. One eye rup-

tured and became atonic by the eight-hour reading; but the others maintained these very low levels of pressure and were not atonic.

At the end of a week the pressure in the eye of the last animal to be killed had reached obtainable levels although it was still hypotonic (fig. 1).

The pressure readings in the nonoperated eyes varied widely. One showed no change. In two animals the readings at eight hours were statistically significantly lower than any preoperative readings. These tensions returned to normal the next day.

The nontreated eye in the animal with the ruptured operated eye showed a marked fall in pressure; and when the animal was killed after operation, intraocular pressure was 12 mm. Hg. The conjunctiva of this eye showed a great deal of chemosis. Such a reaction did not occur in the other animals.

Histologically, the results following cyclo-diathermy over a nine-day period show im-

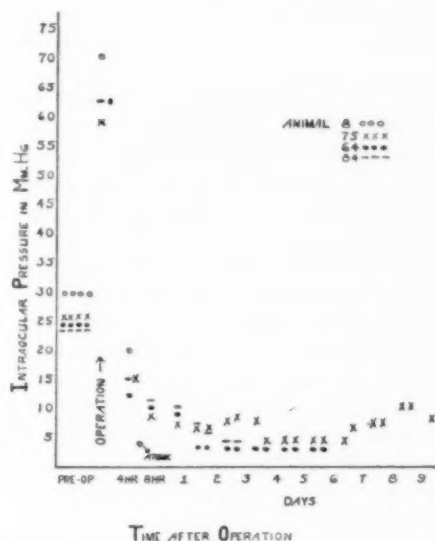


Fig. 1 (Van Heuven and Dunn). Chart, showing range of intraocular pressures.

* From the Department of Surgery, Yale University School of Medicine. Aided by a grant from the James Hudson Brown Memorial Fund of the Yale University School of Medicine.

mediate destruction with gradual clearing and scarring.

The sections taken one day postoperatively show the processes underlying the line of treatment to be necrotic with pigment dispersed throughout areas of hemorrhage. Separation of the pigment layer of the processes is evidence of edema. The angle on this side appears occluded by the swollen, hyperemic iris. Red blood cells and leukocytes are present in the spaces of Fontana. The iris also shows areas of hemorrhage. There is present in the anterior chamber a fine coagulum consisting of red blood cells, exudate, and a few granules of pigment.

Of the processes underlying the nontreated half of the eye some are filled with blood while others show uveal dilatation with edema and hyperemia, as does the iris. The canal on this side, however, appears clear; but there are cells in the spaces of Fontana. The pigment of the processes shows slight clumping.

The sections taken three, six, and nine days later show gradual clearing of the debris on the treated side mostly by way of the choroidal vessels. These processes on the ninth day are an adhered mass also attached to the iris. There is disintegration of the melanophores with marked clumping and dispersion of the pigment. The iris still shows some areas of hemorrhage.

The processes of the nontreated eyes continue to show uveal dilatation with some edema and hyperemia on the third day but, by the sixth day, have returned to normal. There is no evidence on the ninth day of any compensatory uveal dilatation, hyperemia, or hypertrophy of the epithelial cells suggesting increased secretion when the intraocular pressure has begun to return toward normal. The canals appear to be open by the third day and the anterior chamber and spaces of Fontana are clear of exudate and cells by the sixth day.

The processes of the nontreated eyes show some edema as late as the third day but no other changes.

DISCUSSION

We feel that the acute rise in tension must be accounted for as a vascular reaction to the severe stimulus of cyclodiathermy. The immediate rise and sudden decline would seem to bear this out. However, as the uveal dilatation and edema persisted even after tensions had fallen to nonrecordable levels, other alterations must have come about.

It would seem fair to postulate that the enzyme systems and electrical barriers postulated by Kinsey¹ and Friedenwald^{2,3} as regulating aqueous-humor production must be destroyed in those treated areas and reversibly inhibited in the remaining processes. When the reaction subsides, these systems begin functioning again and the pressure returns to normal. The changes in tension in the nontreated eyes can only be explained at this time as a result of a nervous reflex mechanism.

CONCLUSIONS

1. Cyclodiathermy results in an immediate and severe rise in intraocular pressure with a rapid decline in the next four hours to hypotonic levels. This study provides evidence that, after nine days, there is a return toward normal.

2. Histologic sections show gross destruction of the treated processes with eventual scarring and atrophy. The nontreated processes show immediate uveal dilatation with edema and hyperemia but return to normal by six days after operation. There is no hypertrophy of the remaining processes.

3. Debris is carried off via the choroidal vessels for the most part.

4. Physiologic experiments designed to measure the functions of the secretory mechanisms in the epithelium of the ciliary processes would yield much valuable information as to the action of cyclodiathermy in reducing intraocular pressure.

Yale University School of Medicine.

We are indebted to Dr. David Freeman for his invaluable aid in interpreting the histologic sections and to Dr. R. M. Fasanella for his help and suggestion in carrying out this project.

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ENDOPHTHALMITIS
PHACO-ANAPHYLACTIA WITH
GRANULOMATOUS IRITIS*

CLINICO-PATHOLOGIC CASE REPORT

MILTON M. SCHEFFLER, M.D.
Chicago, Illinois

CASE REPORT

Mrs. A. O., a 61-year-old white woman, was a known diabetic of six years' duration. Her ocular complaints were those of gradual reduction in visual acuity to 20/500 in the left eye and counting fingers at one foot in the right eye.

Examination revealed bilateral senile nuclear sclerosis. On February 24, 1949, an intracapsular lens extraction was attempted in the left eye. The lens capsule was broken at the time of the extraction so that considerable cortex was present in the anterior chamber at the first dressing. The postoperative course proceeded uneventfully and the patient was discharged on the ninth day.

She was re-admitted to the hospital on April 25, 1949, because of tearing and redness of the left eye associated with headaches of four weeks' duration. Examination revealed folds of the cornea with a dense aqueous flare and many cell clumps. The right eye exhibited a mild ciliary flush and, within the week, became quite red with corneal bedewing and a definite aqueous flare. The etiologic work-up, including laboratory and X-ray examination, which followed, was normal.

* From the Department of Ophthalmology, University of Illinois School of Medicine and the Illinois Eye and Ear Infirmary. Presented before the Chicago Ophthalmological Society, November 17, 1952.

The patient was given seven courses of intravenous typhoid without much relief of her symptoms. By May, 1949, the tension of the right eye had risen to 48 mm. Hg (Schiotz). Because of the severe pain, the patient was given a retrobulbar injection of procaine. Eventually, following streptococcus vaccine desensitization, the symptoms gradually subsided and she was discharged from the hospital June 12, 1949.

She was next seen November 25, 1949, at Milwaukee County Hospital on the service of Dr. S. Blankstein, because of pain and redness of the right eye. There was edema of the cornea, many large keratic precipitates on the posterior corneal surface, and an aqueous beam with dense posterior synchias. The lens was opaque and quite mature. The intraocular pressure was 50 mm. Hg. The iridocyclitis of the left eye had sub-



Fig. 1 (Scheffler). The inflammatory reaction primarily involves the anterior segment.

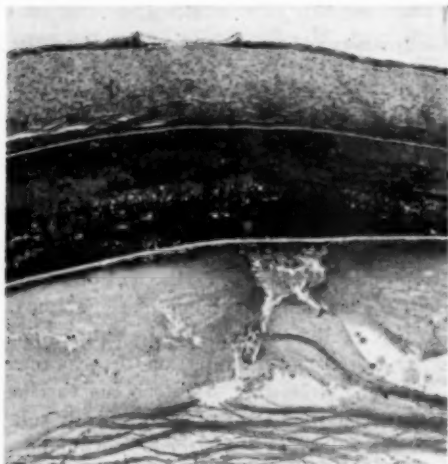


Fig. 2 (Scheffler). The dense, inflammatory exudate of polymorphonuclear cells filling the anterior chamber with the diffuse infiltration of the disorganized iris.

sided but there was a thick secondary membrane in the pupillary area. Further therapy for the right eye, including a paracentesis, was to no avail and an enucleation was performed December 29, 1949.

The clinical impression was sympathetic ophthalmia.

MICROSCOPIC STUDY

The essential pathology was primarily that of an anterior uveitis with the posterior pole relatively normal (fig. 1).

The limbal episcleral tissue was markedly thickened by chronic inflammatory cells, consisting of plasma cells and lymphocytes, with a tendency for nodule formation.

The corneal epithelium was edematous with vesicle formation. There was moderate fragmentation and pyknosis of the lamellar nuclei. In one area, a thin, healed, penetrating wound of the cornea, extending from the limbus obliquely into the anterior chamber, was visible. The defect in Descemet's membrane was occupied by organized inflammatory tissue. This was the site of the paracentesis wound.

The anterior chamber was shallow and

loaded with an inflammatory exudate, predominantly polymorphonuclears (fig. 2). The angles were obliterated with compression of the trabecular spaces.

The iris was diffusely infiltrated with chronic inflammatory cells and replaced in some areas by several granulomatous nodules, resulting in considerable destruction of the iris architecture (fig. 3). The inflammatory cells were predominantly plasma cells and some plasmacytoids.

The granulomatous lesions had broken through the posterior iris surface and were fused by an organizing inflammatory exudate to the anterior lens surface. The cytology of these lesions revealed a central area of fibrosis and some epithelioid cells and several giant cells of the Langhans type showing pigment phagocytosis. The periphery of the nodules revealed a minimum of lymphocytes with mainly plasma cells visible.

The posterior chamber was filled with degenerating lens cortex, many polymorphonuclear cells, and monocytes, as well as giant cells containing pigment particles.

The lens capsule was broken in two places: anteriorly, in the vicinity of the granulomatous lesion of the iris, to which it was adher-



Fig. 3 (Scheffler). The granulomatous lesion of the iris breaking through the posterior pigment layer and the underlying lens capsule broken.

Fig. 4 (Scheffler). The posterior chamber is filled with degenerating lens cortex, polymorphonuclears, macrophages, and an occasional giant cell. The rupture of the lens capsule in the equatorial zone is clearly seen.



ent, and in the equatorial zone (fig. 4). The degenerating lens fibers in these areas were infiltrated with many polymorphonuclears. The cortex was markedly vacuolated (fig. 5).

The choroid was relatively clear with only an occasional area of lymphocytic infiltration anteriorly.

The inner surface of the retina and optic nerve revealed clumps of precipitates made up of macrophages and some polymorphonuclears (figs. 6 and 7). There was some lymphocytic perivascular cuffing of the veins of the retina off the disc.

COMMENT

Microscopically, the diagnosis was not exactly clear cut. The picture was that compatible with a diagnosis of endophthalmitis phaco-anaphylactia. Yet, how could we explain the granulomatous iritis? This is not a part of phaco-anaphylaxis. The probability of two separate disease processes in the same eye presents itself.

Endophthalmitis phaco-anaphylactia, as we know it, is a nongranulomatous uveitis with a disproportionately greater involvement of the anterior uvea. It is usually considered a unilateral disease, although Verhoeff and Lemoine,¹ as well as Courtney,² recognized a bilateral form as existing.

Microscopically, there is a marked polymorphonuclear cell exudation in the anterior chamber. The lens is invaded by polymor-

phonuclear and mononuclear phagocytes through the ruptured lens capsule, as well as giant cells. Posteriorly there are deposits of macrophages and polymorphonuclears on the retina.

The disease is initiated by an allergic response to the lens protein in the aqueous,



Fig. 5 (Scheffler). The lens cortex is vacuolated and infiltrated with polymorphonuclears and macrophages.



Fig. 6 (Scheffler). Clumps of precipitates deposited on the inner retinal layers and optic nerve, with the choroid clear.

whether produced surgically or otherwise, with a superimposed bacterial component.

A second group of cases, phacotoxic, bears some relationship to endophthalmitis phaco-anaphylactia, probably one of degree, and usually occurs in eyes with a mature to hypermature cataract. There is usually a previous history of extracapsular lens extraction in the opposite eye.

A spontaneous defect is present in the lens capsule which allows the degenerating lens cortex to escape into the posterior chamber. The reaction which follows is also primarily an anterior uveitis and is fairly typical. The infiltration in the iris is diffuse, with many plasma cells. The exudation in the anterior chamber and invasion of the lens of polymorphonuclear and giant cells is however at a minimum.

What is the explanation of the granulomatous lesion of the iris? The possibility of sympathetic ophthalmia must be considered since the lesion is located in the posterior iris layers, breaking through and destroying the pigment epithelium with production of posterior synechias.

The nodules show some fibrosis with a central zone of a few epithelioid cells and Langhans type of giant cells. The periphery of these nodules shows no mantle of lymphocytes. The posterior uvea is relatively clear, raising doubt as to the possibility of such a diagnosis.

Clinically, sympathetic ophthalmia is a bilateral disease with both eyes generally involved in a similar process. From the history in this case, the supposedly exciting eye had become symptom free whereas the "sympathizing eye" went on to eventual enucleation. This is not the general course of sympathetic ophthalmia.

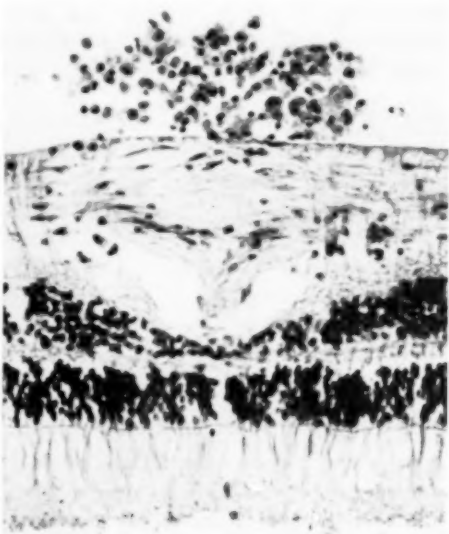


Fig. 7 (Scheffler). High-power view of retinal precipitate with its clumps of polymorphonuclears and macrophages.

The possibility of either Boeck's sarcoid or tuberculosis as the etiologic agent has also been considered but no verification could be demonstrated either clinically or from the laboratory work-up. The microscopic picture of these diseases bears some similarity to the description already given.

The slides were examined by Dr. Verhoeff,³ Dr. Friedenwald,⁴ Dr. Theobald,⁵ and Dr. Klien.⁶

A microscopic diagnosis of endophthalmitis phaco-anaphylactia was suggested by the majority of these doctors, one of whom emphasized the unusual association of the granulomatous iritis and suggested a possible fungus infection, although this did not appear likely. Another expressed the opinion that this was a typical picture of phacotoxic reaction.

Three out of four observers did not be-

lieve this was sympathetic ophthalmia. Dr. Klien,* however, was of the opinion that the case was one of sympathetic ophthalmia superimposed on an endophthalmitis phaco-anaphylactia. Her reasoning has definite merit, yet we were not fully convinced that this was sympathetic ophthalmia for the reasons already stated.

CONCLUSION

A case is presented which, clinically and for the most part microscopically, conforms with the diagnosis of endophthalmitis phaco-anaphylactia but with a superimposed granulomatous anterior uveitis of unknown etiology.

55 East Washington Street (2).

The author is indebted to Dr. S. Blankstein for his help in gathering the pertinent clinical history.

*Dr. Klien's discussion of this paper will be found on page 1460.

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ANTERIOR AND POSTERIOR CHAMBER COMMUNICATION

REPORT OF A CASE

EDWARD O. BIERMAN, M.D.

Los Angeles, California

History. In November, 1941, the patient, then aged 12 years, was struck in the right eye with a missile from an air rifle. A severe inflammation of the right eye followed. He was treated with hot packs for seven weeks and with various ointments and drops. He remained under active treatment for three months and wore a patch for 18 months. He has had poor vision in the right eye ever since.

Examination. The patient's age at the time

of the present examination was 21 years. Visual acuity was: O.D., 20/200; O.S., 20/20.

External examination revealed the cornea of the right eye to be clear and the anterior chamber deep. Posterior and peripheral anterior synechias were present, as was a traumatic cataract.

There was a small opening in the iris which otherwise was completely bound to the lens due to the adhesions. In front of the small opening was a single stroma fiber which oscillated forward and backward. The left eye was normal.

Ophthalmoscopy on the right eye could not be done because of the cataract. The left eye was normal.



Fig. 1 (Bierman). Drawing, showing the position of the stromal fiber and the opening in the iris. The pupil is bound down by adhesions.

REASON FOR STUDY AND METHOD

All observations were made with the Universal slitlamp.

The study of this case was undertaken because a stroma strand in front of the hole in the iris oscillated backward and forward, indicating that at times aqueous went from the anterior to the posterior chamber. The stromal fiber often bent completely behind the iris.

In the first study, I found that the fluid would flow forward on the average of 2.3 seconds and backward, 0.62 seconds. The second observations, approximately one week later, showed that the fluid flowed forward on an average of 2.6 seconds and backward 1.2 seconds. The flow was very irregular. The forward flow varied from 5.0 to 1.4 seconds. The backward flow varied from 0.2 to 1.6 seconds. The oscillations were checked 10 times in obtaining each of the averages.



Fig. 2 (Bierman). Enlargement of the area, showing the stromal fiber.

Relation to accommodation. There was apparently no relationship between the attempted act of accommodation and the oscillation of the fiber. Even though the patient held his gaze at a single point, the fiber continued to oscillate.

Relation to pilocarpine. Pilocarpine had no obvious effect on the oscillation of the fiber.

DISCUSSION

A flow of aqueous from the anterior to the posterior chamber occurred in this patient. The type of oscillation may have been due to the pathologic condition present in this eye, and possibly this mechanism does not function in normal eyes.

5885 San Vicente (19).

USE OF CORTISONE IN PARALYSIS OF OCULAR MUSCLES*

PRELIMINARY REPORT OF TWO CASES

GUILLERMO PICÓ, M.D.

Sanjurjo, Puerto Rico

Cortisone is being widely used, either parenterally or locally, in various eye conditions. Numerous reports have appeared in the literature of its use in diseases affecting one or more tissues of the eye. It is surprising that there have been no attempts to use cortisone in paralysis of the ocular muscles, especially in those cases of undetermined etiology. In a review of the literature, I have been unable to find any mention of the use of cortisone in paralysis of ocular muscles.

The following two cases were presented at a meeting of the Section of Ophthalmology of the Puerto Rico Medical Association.

REPORT OF CASES

CASE 1

I. R. G., a white woman, aged 56 years, was first seen on February 19, 1951, with a

* From the Section of Ophthalmology, School of Medicine, University of Puerto Rico.

history of ptosis and diplopia in the left eye of 12 days' duration. She had had diabetes for several years and it was well controlled with diet.

With the exception of the ocular findings, the general physical examination, including a neurologic examination, was essentially negative. No focus of infection was found.

X-ray films of skull were negative.

Laboratory studies including complete blood count, urinalysis, and blood Kahn were negative. Fasting blood sugar was 130 mg. percent.

External examination of the right eye was negative.

In the left eye, there was a paresis of the levator palpebrae muscle. With maximum effort, the lid was raised to near the upper border of the cornea. There was marked limitation of action of the internal rectus muscle with exotropia of 35 degrees when looking straight ahead. The superior rectus muscle also showed marked weakness. The pupil reacted well to light and accommodation. The other extraocular muscles showed normal action.

Ophthalmoscopy showed some large lens opacities behind the iris, worse in the right eye. The eyegrounds showed only slight retinal angiosclerosis.

Vision was: O.D., 20/70, with correction 20/20-3; O.S., 20/40, with correction 20/25-1.

Visual fields were negative.

A diagnosis of paresis of the levator palpebrae, internal rectus, and superior rectus muscles of undetermined etiology was made.

Treatment was started with intramuscular thiamine hydrochloride, 100 mg. daily for two weeks, therapeutic vitamin formula capsules by mouth, and hot saline compresses to the left eye.

After 48 days with that type of treatment, the degree of paresis of the affected extraocular muscles was unchanged. Then it was decided to try cortisone on the basis that it

might block any inflammatory process, either in the third-nerve nucleus or infranuclear, that could be responsible for the paresis of those muscles.

Intramuscular cortisone in dosages of 100 mg. every eight hours for two days was started on April 3, 1951. She continued with 100 mg. of cortisone every 12 hours for two days and then 50 mg. every 12 hours thereafter.

After 36 to 48 hours of treatment, the improvement was very marked and in five days the paresis of the three affected muscles had completely disappeared.

The cortisone was continued for 11 more days to avoid any recurrence. She received in all a total of 2,000 mg. of cortisone.

Her diabetes remained well controlled during the period of cortisone therapy. Six months later the patient remains well.

CASE 2

L. B. O., a white woman, aged 52 years, was first seen on June 5, 1951, complaining of ptosis of the left upper eyelid, nausea and vomiting, and pain in and around the left eye which extended down to the left side of the nose and the neighboring area of the cheek, of nine days' duration.

A thorough general physical examination done by the internist, who referred the case, was negative.

X-ray films of skull were negative.

Laboratory studies including blood Kahn, urinalysis, and complete blood count were negative except for slight hypochromic anemia.

Examination by the otolaryngologist revealed a possible ethmoiditis but no local treatment was given to the nasal condition.

X-ray films of teeth were negative.

The external examination of the right eye was negative.

In the left eye there was a paralysis of the levator palpebrae and of all the other extraocular muscles except the external rectus muscles. The left pupil did not react to

accommodation and reacted poorly to light.

Examination of the eyegrounds showed only slight narrowing in the retinal arteries in both eyes.

• Vision was: O.D., 20/200, with correction, 20/20; O.S., 20/200, with correction, 20/25.

Visual fields were negative.

A diagnosis of paralysis of the third and fourth nerves and probable partial trigeminal neuralgia was made. Having had excellent results with the first case reported here, cortisone therapy was started on June 7, 1951, two days after the patient was first seen.

Intramuscular cortisone was begun in dosages of 100 mg. every eight hours for two days. She continued with 100 mg. of cortisone every 12 hours for two days and then 50 mg. every 12 hours thereafter.

Thirty-six hours after starting the cortisone, she was able to elevate the left upper lid to just above the pupillary area. The pain and the nausea and vomiting also disappeared. By then, there was also slight action of the other extraocular muscles that were paralyzed. The action of the paralyzed extraocular muscles rapidly continued to improve and the diplopia to diminish.

On June 16, 1951, nine days after starting

the cortisone, the extraocular muscles had regained their total function and the diplopia disappeared. The pupil also reacted well to light and accommodation. The cortisone was continued until she had received in all a total of 2,500 mg.

Vision was 20/20 with correction and she could read the smaller Jaeger print at the end of the treatment. Five months afterward the patient remains well.

SUMMARY AND CONCLUSIONS

The use of cortisone in paralysis of ocular muscles has apparently never been tried before.

Two cases with paralysis of ocular muscles of undetermined, but probably inflammatory, etiology and treated successfully with cortisone are here reported. Although the number of cases is small, I believe that the excellent results obtained justify this preliminary report.

I wish to stimulate interest in using cortisone in paralysis of the ocular muscles so that its efficacy may be completely evaluated in cases with different etiologic factors.

Avenue Ponce de Leon 654.

OPHTHALMIC MINIATURE

Although the roots of the cilia appear to be disposed in one line only, they nevertheless form two, three, and in the upper lid even four ranges of hairs, unequally situated, and as it were confused. Whenever, therefore, in consequence of disease a certain number of hairs are separated from each other in a contrary direction and disorderly manner, the eyelash will appear to be composed of a new and unusual row of them, while in fact there has been no change either with respect to their number or natural implantation.

Antonio Scarpa, 1801.
(From Brigg's translation.)

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

CHICAGO OPHTHALMOLOGICAL SOCIETY

November 17, 1952

DR. WILLIAM F. HUGHES, JR., *president*

The clinical meeting was presented by the Departments of Ophthalmology, Chicago Medical School, and Michael Reese Hospital, Dr. Paul Sternberg presiding.

SUSPECTED TOXOPLASMOSIS

DR. IRVING D. HOROWITZ presented S. C., an eight-year-old Negress, who was brought to the Michael Reese Eye Clinic with the complaint of faulty vision in the right eye since birth, associated with right convergent strabismus. Past medical and family history were negative.

Examination revealed corrected vision of 20/200, R.E., 20/60, L.E. There was bilateral nystagmus and right convergent strabismus. A fairly large, healed, central chorioretinitis was noted in the right eye with diffuse areas of depigmentation surrounded by pigment clumps in other quadrants of the fundus. The disc was quite pale suggesting optic atrophy. The left fundus was essentially negative.

Because of the negative history for disease or injury the possibility of congenital toxoplasmosis was considered. A skin test was positive at the 48-hour period. The result of the blood neutralizing antibody tests has not yet been returned from the state laboratory. No calcification was demonstrated in the skull films.

A chest survey also proved negative.

Although there is a tendency to rely upon the blood neutralizing antibody test, Heidehman concluded that the presence of neutralizing antibodies should be considered of only moderate diagnostic value and their absence does not rule out the possibility of toxoplas-

mosis infection. Hogan believes the chief significance of the test lies in the ability to demonstrate a rising titer.

The ocular lesion of toxoplasmosis is a necrotizing one, beginning with intense edema and congestion which distort the retinal layers. In the more central portion of the lesion necrosis of all retinal layers may occur, whereas in the periphery only the innermost layers of the retina are involved.

Perivascular and diffuse infiltration by inflammatory cells is easily demonstrated in the marginal areas. The cellular infiltration consists chiefly of lymphocytes and large phagocytes but may also contain plasma cells and occasional eosinophils and polymorphonuclear leukocytes. Intracellular bodies have been found in some of the macrophages and probably represent the organism.

The choroidal inflammation is usually not as intense as that found in the retina. The sclera is characteristically not involved. The organisms can be found in the retinal lesions, being more prevalent where the inflammation is severe. They may exist singly or in clusters, free or intracellularly, or as pseudocysts. They are rarely found in the choroid.

The initial site of infection is still unknown and the method of ocular involvement is still not clear. The diagnostic importance of chorioretinitis whenever toxoplasmosis is suspected is emphasized.

INCARCERATION OF IRIS

DR. IRVING D. HOROWITZ said that E. F., a 66-year-old white woman, had had a right intracapsular cataract extraction with a complete iridectomy in March, 1950. The corrected vision of this eye was 20/25. However, a small iris incarceration covered by conjunctiva was noted at axis 120.

The patient presented herself on February 11, 1952, with a red, painful right eye of two days' duration. Vision was light perception only. There was a purulent conjunctivi-

tis. The cornea was edematous, a four-mm. hypopyon was present in the anterior chamber, and the vitreous contained massive exudative material. Only a faint fundus reflex was noted with the ophthalmoscope and tension was elevated to 38 mm. Hg (Schiotz). A diagnosis of acute purulent endophthalmitis was made and the patient was hospitalized. Culture revealed hemolytic, coagulase positive *Staphylococcus aureus*.

The following therapy was administered:

1. Immediate subconjunctival injection of one million units of penicillin and daily thereafter for six days.

2. Chloromycetin orally, 1.5 gm. daily, in divided doses for nine days.

3. Aureomycin and atropine drops, penicillin ointment, and continuous hot compresses locally.

4. Four injections of typhoid vaccine, increased progressively from 25 to 200 million units.

The corneal edema gradually disappeared, the anterior chamber and the vitreous cleared, and vision slowly improved; at present it is 20/30. Chloromycetin ointment is being used in the right eye each night. It is intended to excise the incarceration with careful closure of the wound at its site in order to eliminate recurrence, and it is believed that all incarcerations or prolapses should be so cared for at the time they occur.

Discussion. Dr. Samuel Schall noted that this complication occurred almost two years following lens extraction. During this interlude one may assume that any pathogenic organism that might have caused conjunctivitis was either effectively controlled by the antibacterial action of the tear lysozyme or the thinned conjunctiva over the iris prolapse proved sufficient barrier. A breakdown of these due to overwhelming and highly pathogenic infection resulted in endophthalmitis.

When this patient was first seen, the corrected visual acuity was less than 20/400. The eye was severely injected, especially about the site of iris prolapse. The vitreous

was hazy with a localized abscess-like collection in the vitreous below at the 6-o'clock position. In a few cases of this type previously seen, the eye was either lost or went on to phthisis bulbi no matter what treatment was employed.

Treatment usually included iontophoresis with penicillin and streptomycin, or direct intravitreal injection of recommended doses of these drugs, as well as the usual supplementary treatment. The experience with such infections has been discouraging.

When the stained microscopic slides of an eye lost from postoperative endophthalmitis are examined, it is obvious that nothing could have saved the eye. The vitreous body is either filled with pus or portions are infiltrated with polymorphonuclear leukocytes, or the retina may be infiltrated and there may be an organizing exudate present. The excellent outcome of the case presented here was undoubtedly due to the expeditious manner in which treatment was carried out. The therapy was based largely on the recommendations of Sorsby and Unger, reported in the *British Journal of Ophthalmology* in January, 1950.

In cases of this type, the best cure is prevention. Prolapsed iris with a thin conjunctival flap should be repaired immediately. When the prolapse is well established and covered with thin conjunctiva, it is important to keep the patient on an antibiotic such as sulamyd or chloromycetin for the remainder of her life. Late repair of the iris prolapse may be indicated but, in any case, the patient should be kept under observation.

BAND-SHAPED KERATOPATHY AND GLAUCOMA

DR. MARTHA RUBIN FOLK presented B. O., a 50-year-old white man, first seen at the Eye Clinic of Mt. Sinai Hospital on November 10, 1947, with complaint of failing vision of several months' duration and sensitivity to light.

This patient had an active duodenal ulcer of 25 years' duration, for which he had taken

excessive amounts of milk and alkali, but from which he had suffered repeated episodes of chronic gastrointestinal bleeding. In March, 1947, he had been admitted to the hospital in a state of shock from acute blood loss with resulting renal shutdown and marked azotemia, which responded to conservative therapy. The patient's mother had bilateral glaucoma and hypertensive vascular disease; the father has arteriosclerotic heart disease.

Examination at this time showed vision, R.E., 20/40; L.E., 20/30. There was moderate injection of palpebral and bulbar conjunctivas. Both corneas showed fine white subepithelial deposits adjacent to the limbus, extending to the cornea some two to three millimeters, with a clear zone intervening. These deposits were confined primarily to the interpalpebral zone, although there was some extension beyond this. The chambers were slightly shallow. There was mild retinal sclerosis. Tension was: R.E., 22 mm. Hg; L.E., 20 mm. Hg (Schiotz). Corrected vision was 20/20 in both eyes.

When seen again on March 12, 1948, it was felt that there was a slight increase in the corneal pathology.

He did not return to the eye clinic until May 3, 1952. During this time he had been on medical management of the ulcer and had had repeated transfusions for chronic anemia and azotemia. Surgery was refused until April, 1951, when a gastroenterostomy was done. He did well for six months until he developed a stomach ulcer which started the cycle again.

Vision at this time was 20/30, R.E., 20/25, L.E. The corneas showed increase in the opacities previously described. The anterior chambers were very shallow. The fundi showed a normal disc in the left eye and moderate glaucomatous cupping in the right eye. Tension was: R.E., 45 mm. Hg; L.E., 21 mm. Hg.

Central fields showed enlargement of the blindspot in both eyes, and Seidel scotoma

and constriction in the right eye. Gonioscopy shows the angles to be open to most of the pigmented trabeculae, but a very broad iris hump.

Tension has been fairly well controlled in the left eye but poorly controlled in the right. X-ray films of the globes reveal them to be calcified; despite this, the scleral rigidity is low in both eyes.

The pathogenesis of diffuse metastatic calcification in this case, of which the corneas and conjunctivas are only one part, is believed to be some type of pre-existing renal disease with further renal damage from hemorrhage, shock, and dehydration, resulting in chronic renal insufficiency and inability of the kidneys to handle alkalis. This with chronic vomiting and excessive intake of alkali has resulted in hypochloremia and metabolic alkalosis.

It is not felt that the glaucoma bears any relation to the metabolic disorder, although it is conceivable that calcification of the trabeculum may play a part. Bilateral iridocleisis is indicated, but surgery has been deferred in view of the patient's poor condition, and the possibility of complications resulting from the diffuse calcification of the eye and blood vessels.

UNILATERAL OPTIC ATROPHY

DR. HAROLD C. LEIGHT presented L. J., a 14-year-old Negro, who poses a problem of progressive loss of vision in the right eye with no obvious etiology or physical findings. He was first seen at the age of 10 years for routine examination, at which time refraction revealed an error of +2.5D. sph. in each eye. On examination two years later a discrepancy between the cycloplegic and post-cycloplegic examination was attributed to accommodative spasm and glasses were not prescribed.

In April, 1952, the patient complained of poor vision. Unaided vision was: R.E., 20/100; L.E., 20/25. Homatropine refraction showed no change and postcycloplegic

revealed: R.E., +0.5D. sph. \ominus +25D. cyl. ax. $90^\circ = 20/80$; L.E., plano +25D. cyl. ax. $90^\circ = 20/20$. A pinhole did not improve vision in the right eye.

In September, 1952, the right vision is recorded as: R.E., 20/100; L.E., 20/25. Ocular examination is still entirely negative except for minimal temporal pallor of the right disc.

Visual fields showed normal peripheral field but central scotoma for two-mm. blue and relative scotoma for two-mm. red in the right eye at the fixation point.

Blood Wassermann test is negative. Skull X-ray films showed the right optic foramen smaller than the left. Neurologic examination was negative except for marked nystagmus on extreme lateral and medial gaze.

Because of the minimal findings a definite diagnosis is difficult at present. Multiple sclerosis and Leber's disease might be considered but, in case of the latter, the opposite eye would have been affected by this time; also, no familial history has been elicited.

Congenital syphilis should be considered as a possible cause of optic atrophy in the young; if arrested early, a positive Wassermann reaction may not be shown. Another possibility is that the patient may have had a mild convergent squint in early childhood which has since disappeared. There was a high esophoria when he was first seen at the age of 10 years, which has decreased; also there is a tendency to accommodative spasm. However, the recorded visions show a decrease from 20/40 to 20/100 since being followed in the clinic in the absence of squint or suppression.

SCIENTIFIC MEETING

ENDOPHTHALMITIS PHACO-ANAPHYLACTIA

DR. MILTON M. SCHEFFLER presented a clinicopathologic report of a case of endophthalmitis phaco-anaphylactia associated with granulomatous iritis. His paper is published in full on pages 1449 to 1453 of this issue of *THE JOURNAL*.

Discussion. Dr. Bertha Klien: During the past few years the concept of lens-induced inflammation has been crystallizing more and more, not only from a histopathologic but also from a clinical point of view. Prompt removal of the offending lens now saves eyes which previously would have been lost. The clinical differential diagnosis from other conditions, especially from sympathetic ophthalmia, is not always easy. The histologic picture is more clear cut, yet all its ramifications are not as yet known. There is, for example, the question of the co-existence of other types of inflammation.

There are two cases in the literature in which sympathetic ophthalmia was associated with lens-induced inflammation and, at Northwestern University Laboratory of Eye Pathology, there is one eye which came from a patient suffering from chronic tuberculous uveitis. The uveitis had quieted down after several years, but in one eye secondary glaucoma developed for which a surgical procedure was carried out.

During the operation the lens, unknown to the surgeon, was injured, and the subsequent inflammatory process in this eye was interpreted as recurrence of the tuberculous process. The eye, which did not have useful vision, was removed, and histologic studies revealed a typical picture of lens-induced inflammation superimposed upon an old, apparently not active granulomatous uveitis. The co-existence of two conditions in the pathogenesis of which allergy or hypersensitivity play a role is really not surprising.

In Dr. Scheffler's case there also seems to be a co-existence of two conditions, an anaphylactic type of inflammation with a specific granulomatous process—whatever the latter's nature may be.

The clinical data which would be most interesting to the pathologist in such cases are: descriptions of both lenses, if there were or are cataracts and, if so, were or are they mature, immature, or hypermature.

As the matter stands now, the condition of the lens of the injured eye, or of the op-

erated eye with a lens injury prior to operation, does not appear to matter much in the development of lens-induced inflammation. However, up to now, we are not justified in making the clinical diagnosis of lens-induced inflammation in an uninjured eye with a spontaneous inflammation, unless the lens is at least mature or hypermature.

This, of course, calls for a clearcut definition of what constitutes a hypermature cataract. Could it be that circumscribed lamellar separation or water clefts, which may persist for many years almost without progression in an immature lens, may develop leakage of toxic substances and constitute partial hypermaturity of the lens, with subsequent lens-induced inflammation?

Questions like this will have to be answered before the picture of lens-induced inflammation is complete, and before clinical appraisals of situations arising from it are materially aided.

Dr. William F. Hughes, Jr.: The granulomatous feature which Dr. Scheffler demonstrated pathologically can also occur clinically. In a series reviewed with Dr. Owens some years ago, it was found that mutton-fat keratic precipitates were not uncommon in apparently lentogenic uveitis.

Dr. Milton M. Scheffler (closing): These slides show a case of primary glaucoma in which an iridencleisis was performed. The lens was accidentally injured, followed several months later by uveitis, with eventual enucleation of the eye. Here is shown a somewhat different reaction in which the lens itself is infiltrated with many giant cells, whereas the case just shown had none at all.

The picture of the iridencleisis wound shows the area in which the capsule was apparently nicked. The lens is markedly infiltrated with polymorphonuclears as well as giant cells. The next slide reveals the lens again; the connective tissue formation which lies just underneath the capsule is also heavily infiltrated with polys. The higher power shows polymorphonuclears lying on the anterior lens surface, with the giant cells visible

in the lower end, proliferating within the lens itself. This is of course a somewhat different picture from the one previously shown, and is a typical picture of endophthalmitis phaco-anaphylactias.

ANISOPHORIA, ANISOMETROPIA, AND THE FINAL PRESCRIPTION

DR. JAMES E. LEBENSOHN presented a paper* on this subject, a summary of which follows:

In 200 consecutive cases of anisometropia, hyperphoria was tested for distance with eyes level and in the reading position of downward gaze without corrective lenses. The correct interpretation of vertical anisophoria requires this simple and informative method. In almost two thirds of the entire group, the intrinsic anisophoria effected a mitigation of the anisometropic anisophoria either automatically or by the prism correcting the distance hyperphoria.

The prevailing types of anisophoria simulated a weakness of either the superior oblique or the superior rectus of the eye with the more myopia or less hyperopia in the vertical meridian.

The influence of intrinsic anisophoria should be reckoned in all calculations concerned with devices for neutralizing anisometropic anisophoria. A size difference, obtainable with readily available lenses, may prove on occasion a valuable aid in combatting either intrinsic or anisometropic anisophoria.

Discussion. Dr. Daniel Snyder: Some of Dr. Lebensohn's terminology differs from that usually employed; the term "intrinsic hyperphoria" as contrasted with "induced hyperphoria" is certainly a clear expression. The principal problem involved is that of fusion.

The devices and mechanisms which he advocates are designed to give satisfactory binocular vision to the individual. If this can

*Published in full in *THE AMERICAN JOURNAL OF OPHTHALMOLOGY*, 36:643 (May) 1953.

be done with comfort and without creating a cosmetic problem, it is worthwhile; by cosmetic problem is implied any cumbersome or unsightly spectacle lens. If comfortable satisfactory binocular vision cannot be achieved by the methods he has described, then, to quote Lancaster, it may not be worthwhile trying to "force on the patient the somewhat dubious advantages of binocular vision."

There are several philosophic implications in the type of therapy employed. If the patient actually has symptoms and is in distress, and his distress can be relieved, he will certainly continue with the therapy. If, on the other hand, he feels reasonably comfortable without therapeutic methods, but it is felt that he may be better off by trying to force binocular vision on him, he may very well object to the type of therapy employed. In such case his neurosis will have to be severe if he puts up with a form of therapy that is worse than the condition of which he complains.

The importance of distinguishing between the types of hyperphoria should be emphasized. One must be sure that a hyperphoria is not induced, and the proper way to do this is to measure the patient's vertical phorias without any correction in place. A few years ago I emphasized the importance of measuring hyperphoria in the various cardinal positions of gaze. This procedure is still followed and has been found eminently satisfactory in making diagnoses, since it sometimes gives valuable clues as to the individual elevator or depressor involved.

Dr. Thomas D. Allen congratulated Dr. Lebensohn on this interesting essay, especially because of his insistence upon testing the hyperphoria for distance in the primary position, and hyperphoria for reading with the eyes down as they usually are when one reads.

Another thing which is important, when one is uncertain as to whether or not hyperphoric correction should be ordered, is to put the glasses in a trial frame accurately centered and let the patient wear it in another

room, for distance and later for reading.

Often, as Dr. Lebensohn suggests, and quotes Scobee, the prism is gratefully borne. If the patient notices the difference between the glass with the prism on, and with the prism off, an effort is made to learn which is more comfortable. The two eyes are tested at the check-up of the glasses to see if there is any hyperphoria with a stereoscopic slide.

Often one is at a loss to know whether or not to order a vertical prism. This difficulty was encountered with a close friend for whom prisms were ordered (he had a little anisometropia) and he was fairly grateful. Then the prism was left off and he was quite uncomfortable for a year or two until it was put back again. Often a hyperphoria is inconstant; it may be seen at one time on examination and not at the next examination.

I developed a hyperphoria at one time rather suddenly, apparently without any cause, which lasted for about two months. A hook-over prism was fitted for my glasses to see whether or not this would last. As suddenly as it developed, it disappeared several months later and has not reappeared.

These eyes of ours are interesting organs, and it takes a good deal of thought to make people comfortable with glasses.

Dr. Derrick Vail was much interested in Dr. Lebensohn's discussion. Most men have had the same experience with vertical imbalances and the decision whether or not to order prisms. Sometimes patients are perfectly contented without prisms and again, as Dr. Allen brought out, they are only happy when the prism is put in. Dr. Lebensohn has helped clarify our thinking along this line.

Dr. Lebensohn's method of reading with the eyes pointed upward could be carried to absurd lengths. If a prism base-up is used, the eyes are in the up position and are divergent; so in addition to vertical phoria there is a physiologic divergence. A prism base-in must be used to bring the reading

focus in the proper line, and a bifocal segment reversed, upside down, and if it is a plus lens the prism will be a vertical prism in the plus lens.

When Dr. Lebensohn looked skyward in reading, when the book was on the desk, one wonders what he was doing with the size differences and with the prism. It would be interesting to hear how he compensates for the reverse of the physiologic gaze.

Dr. James E. Lebensohn (closing): The "Prisma Glasses" with which the paper was read were intended originally as bed spectacles. It is a simplified model which can be used over one's reading correction. The elaborate type still made by Hamlin of London embodies the individual prescription and compensates for the complicating factors that Dr. Vail quite correctly considered. Actually, in the comparatively short period of use, there were no difficulties, and had the manuscript been manipulated more carefully, probably the eyes would have assumed a more natural position. These glasses, which were obtained at the last Academy meeting, are made by American Prismatic Glasses, Inc., of Boston, and are extremely reasonable in price.

Dr. Allen has noted undoubtedly the numerous vague and contradictory statements on handling vertical prisms. The diverse suggestions include a more or less arbitrary reduction of the full prismatic correction, and the advice to place the prism in the lens that is thinnest, or to divide the prism between the two lenses. If one considers separately the precise nature of the intrinsic hyperphoria and the effects induced by the lenses, he can readily figure whether the prism can be tolerated and to what extent it should be utilized. The prism should be placed in the lens for the nondominant eye whenever possible. If one eye fixes for distance and the other for near, the prismatic power is divided, allotting the smaller amount to the eye with the keener and more critical vision.

Dr. Snyder's sympathetic discussion is appreciated because of his deep interest in

all problems related to muscles and refraction.

One speaks of "symptoms" but how reliable is the opinion of an eye-conscious patient with asthenopia as to whether a prism does or does not improve his visual comfort? The ophthalmologist who has all pertinent data at hand can assume the responsibility with assurance.

Some patients learn to wear a new prescription readily; others require considerable time. Consequently, a prescription based on adequate examinations should be changed rarely if ever. For the psychosomatic complaints often encountered, an eight-ounce bottle of elixir triple bromides is prescribed—enough to last until these complaints vanish.

Richard C. Gamble,
Recording Secretary.

NEW ENGLAND
OPHTHALMOLOGICAL
SOCIETY

410th meeting

January 21, 1953

DR. ANDREW L. MACMILLAN, JR., *presiding*

VIRUS DISEASE OF THE CORNEA

DR. ALSON E. BRALEY of Iowa City, Iowa, speaker of the evening, discussed virus diseases of the conjunctiva and cornea.

Epidemic keratoconjunctivitis has a sudden onset with pain, tearing, and edema of the conjunctiva. There is no purulent discharge. Follicles then develop associated with a mucoidlike discharge and a swollen preauricular node. A pseudomembrane develops, caused by a necrosis of the superficial epithelial cells.

The typical corneal opacities are superficial, occurring in or near Bowman's membrane under the epithelium, and rarely stain with fluorescein. These corneal opacities may represent colonies of the virus in the corneal epithelium.

The patient's own blood serum, used as eye drops every half hour, reduces edema and makes the patient more comfortable. Two and one-half percent cortisone in zephiran is helpful in preventing corneal opacities.

The virus of epidemic keratoconjunctivitis is probably an intranuclear virus, epithelial-tropic, and closely related to the viruses that cause encephalitis.

Superficial punctate keratitis usually causes photophobia and foreign-body sensation. The bulbar conjunctiva is slightly injected and dilated vessels are seen coming down from the region of the superior rectus muscle.

The corneal lesions are almost entirely epithelial. They start as extremely small dots of infiltration, which gradually increase in size. The center of the lesion frequently produces a filamentous form which is soon knocked off leaving an oval lesion with a center that stains with fluorescein. The individual lesion recedes leaving a tiny bump which eventually entirely disappears—but tends to recur.

Dr. Braley has isolated a virus from the lesions and has prepared a vaccine which has been of some value in treatment. The local use of cortisone helps to clear up individual attacks and makes the patient feel better.

Herpes simplex corneae manifests itself in four forms:

The first form is most common in teen-age children who have never had herpes before. They develop a bump on their skin, a conjunctivitis, a swollen pre-auricular node, and may develop a dendritic ulcer on the cornea.

The second form of herpes simplex is the self-limited, recurrent, dendritic keratitis that is seen commonly and may occur with or without any conjunctivitis.

The third form is disciform keratitis, which Dr. Braley believes may develop as a local hypersensitivity reaction in the corneal stroma between the herpes virus, acting as an antigen, and local aggressins.

The fourth form is metaherpetica, which usually involves a large area of the cornea, with piling up of the surface epithelium, scarring, and vascularization.

Herpes zoster ophthalmica is an involvement of the ophthalmic division of the fifth cranial nerve with characteristic skin and corneal lesions which are probably hypersensitivity reactions to the virus. Herpes zoster is thought to have a close relationship to chickenpox. The "Ramsey Hunt" syndrome was mentioned, in which herpes zoster involves the seventh nerve causing skin eruptions in the ear and a paralysis of the muscles supplied by the ophthalmic branch of the seventh nerve. The corneal lesions of herpes zoster may occur in all the layers of the cornea and in close association with the corneal nerves.

Molluscum contagiosum, occurring on the lid margins, is often associated with conjunctivitis and a keratitis epithelialis. If the molluscum is present on the upper lid, a pannus may develop in the upper cornea.

Lymphogranuloma venereum may produce a keratitis and may cause a severe destruction of the entire eye.

Slides were shown demonstrating a trachomatous pannus and keratitis.

Inclusion blennorrhoea produces a severe conjunctivitis caused by a virus that belongs to the lymphogranuloma group.

Discussion. Dr. Henry Allen of Boston: I think it must be very hard for any of you who have not worked with viruses, even as little as I have, to appreciate the immense amount of labor that goes into even a simple neutralization test with a virus. Dr. Braley brings to us the benefit of his experience, both in the laboratory and in the clinic, and has certainly made a most stimulating presentation, which I feel woefully inadequate to discuss.

As a result of these same technical difficulties, there is a grave responsibility on those who are investigating the diseases of the eye as to the validity of their conclusions, since there are so very few who are in a position

to question or contradict them; and I think we can rely on Dr. Braley's conclusions in the main.

I was much interested in many of them, in particular with herpes simplex. I must say that Dr. Braley seemed to provide some ready answers and very ingenious theories to problems that have been troubling me for some time. I think his theory of the interpretation of disciform keratitis as a hypersensitivity reaction between the virus and the antibody is certainly a very ingenious one.

The role of fixed or tissue antibodies has been, as Dr. Braley pointed out, a controversial one. They are difficult to demonstrate, and I would like to ask him whether he has any evidence as to whether there is any inhibitory effect on the free virus by such alleged fixed or tissue antibodies.

The identification of the antiherpetic and other antibodies in the gamma globulin fraction is certainly an accurate one as far as the circulating antibodies are concerned. Just what the role of circulating antibodies, that is, circulating neutralizing antibodies is in the clinical immunity to the disease is an interesting problem and also an elusive one.

As Dr. Braley pointed out tonight, as well as in his article, individuals who are not subject to herpes have no herpes antibody, except for the complement fixation antibody, which is something that I have had no experience with and which is news to me. It would suggest, of course, that there was some latent infection which had not appeared clinically; and I think that is a point on which I would like some further elucidation.

We are faced with a virus which is intracellular and which is intranuclear. The heaping up, I believe, does appear very early in sections of rabbit eyes. As the last pictures showed, the virus of herpes simplex seems to be in the nucleus—actually in the nucleus—where, of course, it is very inaccessible to any circulating antibodies, but may be, perhaps, more accessible to fixed antibodies—if there are such in the epithelial cells. However, Dr. Braley stresses the point that these

are located primarily in the stroma rather than in the epithelial cells.

I have tried repeatedly to demonstrate these acidophilic bodies in smears and scrapings of dendritic figures without success. They are very beautifully demonstrated in biopsy sections which run throughout the nucleus, which cut it right through and through, passing to the chromatin envelope and to the inclusion body itself.

I would like to ask Dr. Braley what actual evidence he can bring forward for the theory that this disciform keratitis is an example of an antibody reaction, and I want to conclude by again congratulating him on his very interesting presentation.

Dr. David Cogan of Boston: The entity which we have come to call superficial punctate keratitis consists of spots in the cornea such as Dr. Braley has demonstrated; but I believe the entity which most of us around here call that is an entity that exists for a long period of time, for years, in eyes which are usually white and quiet—and I think this differs a little bit from that which Dr. Braley describes. It is rather hard to consider this a virus disease, at least an acute virus disease, if it does persist for a long period of time.

Dr. Braley specifically said that there was no response to cortisone; but this entity which we call superficial punctate keratitis, I thought was the one eye condition which always did respond dramatically to cortisone. Maybe not to cortisone two or three times a day but when using it often enough. I think it was a very co-operative patient of Dr. Verhoeff who recently had the typical picture of superficial punctate keratitis. Using cortisone three times a day did not have any effect but using it every hour made the spots disappear. Stopping, it would recur.

We did this several times, and it could be made to come and go with cortisone. That patient and others with the same disease have been quite dramatically relieved by cortisone.

Dr. Braley said that patients with superficial punctate keratitis complain bitterly of pain. I had thought it was remarkable how

little they complained of pain. In fact, I know of at least one patient who just seemed to get these spots—they were numerous, 20 or 30 or 50 of them—that were just picked up on routine examination. He had no complaints referable to the eye. I am curious to know whether what we call superficial punctate keratitis does differ from what Dr. Braley calls superficial punctate keratitis.

I would like to ask Dr. Braley if he feels that epidemic keratoconjunctivitis can occur sporadically. We have had several patients with the so-called epidemic variety, and there has been no epidemic.

Dr. Frederick Verhoeff of Boston: Years ago, Fuchs described a definite disease which he called superficial punctate keratitis. It occurred generally after a disease such as bronchitis, and there were superficial spots on the cornea—some of which were as large as a millimeter. His description does not agree with any of the things described here tonight. He never mentioned a pre-auricular gland. I used to see the disease, but I am not sure I see it any more. I once published a histologic case showing the lesions. There is much confusion about the use of the term, superficial punctate keratitis, and I hope Dr. Braley can solve this problem of nomenclature.

I would also like to ask Dr. Braley how he explains the morphology of the dendritic figure. Does he think that represents a nerve distribution? Can he explain the morphology of the disciform lesion? A typical disciform lesion has a little dot in the center of it, and a ring around it. I think most people in talking about disciform lesions absolutely ignore this—anyway, they don't explain it.

Dr. Braley: I must say some very good points have been brought up. Now, to begin with Dr. Allen's question about the ground cornea. We have followed the work done by Thompson, in which he ground corneas and demonstrated antibodies to typhoid. We have used the complement fixation technique and, in some instances, have demonstrated something present in the cornea, which has been called "aggressin" by Rhodes and Van Brugh

and which I assume is an antibody. I believe circulating antibodies have nothing to do with herpes disease so far as the eye is concerned.

I have absolutely no evidence, other than clinical, about the development of disciform keratitis. I feel that, since disciform keratitis is so benefited by cortisone, it must be a hypersensitivity reaction and, therefore, dependent upon the presence of antibodies in the cornea.

Now, as far as terminology is concerned—I must say I am confused too. I don't know what I mean by superficial punctate keratitis. I don't believe anybody else does, because I hear everybody talking about the keratitis of staphylococcus conjunctivitis as being superficial punctate keratitis. Well, of course, I know that it isn't. The thing is an epithelialis; that is what we mean.

I do not know what the disease is that we have here. I know it is not Fuchs's disease—I realize that—and I know that the name is wrong. I don't know what else to call it. I have been calling it Mills's disease, because Mr. Mills was the man from whom I isolated the virus the first time; and I have only found it in about nine or 10 cases.

Now, not all of these people with this clinical picture, which I have tried to show, have antibodies to my virus. It is a chronic disease—there isn't any doubt about that—and it is a chronic type of virus disease. It is not an acute virus disease, and it is the most amazing thing what their neutralizing antibodies do. They go up and down all the time. I have found patients, in doing the population study, who, to my mind, never had anything wrong with them so far as their eyes were concerned, who had neutralizing antibodies to the virus. Some of my patients with this disease, who I am sure have neutralizing antibodies, are helped with cortisone if they use it often enough. They are helped for a period of time, but they may have a flare-up while they are using cortisone. Then, I think some of the flare-up depends upon the presence or absence of their neutralizing antibodies. I don't know for sure about that.

I think you do get sporadic cases of epidemic keratoconjunctivitis. That is one reason why I think it may be closely allied to St. Louis encephalitis. Pre-auricular lymphadenopathy is almost always present in epidemic keratoconjunctivitis. I thought for a time that Fuchs was describing the end result of epidemic keratoconjunctivitis, and I think that Thygeson still thinks so. I don't know what he described; I don't believe I have ever seen the entity as he described it.

The reason for the morphology of the dendritic figure—I don't know—I have some theories about it; but I would just a little bit rather not present them. I think I know why it follows along that pattern. Perhaps I will say just a little about it. This virus spreads in the epithelium; and, histologically, if you carefully examine the corneal epithelium of any normal cornea, you can see that the nuclei seem to be arranged in a certain pattern, particularly in the polygonal cells. Those cells are about three layers up from the basal layer, and the nuclei tend to be oval. I believe that the spread of the infection is one of continuity rather than following nerves. I don't believe that herpes simplex is actually an infection of the corneal nerves.

At the present time in the treatment of herpes zoster, I think the best therapy is probably cortisone. In my hands, cortisone is given parenterally either by mouth or by injection. It is probably the best form of therapy. I cannot tell you the exact time to start it; I usually start it when I see the patients. If it makes them worse, I stop it. If it helps them, I continue it.

Dr. Cogswell: Does that apply only when there are lesions in the eye itself?

Dr. Braley: No, I use it because the lesions around the eye can be extremely painful, you know, and the pain will persist. I know that it brings considerable relief from pain.

Dr. Frederick Verhoeff: How about using aureomycin for herpes zoster?

Dr. Braley: Aureomycin, if it is given in tremendous quantities and intravenously, is

helpful sometimes for the pain. It may relieve the pain. Or, it can be given in large quantities by mouth with some help. Nausea results whether it is given intravenously or by mouth.

Dr. Cogswell: Do you give it in the presence of just a skin lesion—do you still start them on cortisone?

Dr. Braley: Well, I try it, parenterally or by mouth. Try, at least. The last case I had was in a three-year-old child—the ophthalmic division was affected—and followed very shortly after chickenpox. That is, he had the chickenpox, then the rest of the family had chickenpox; and this child came down with herpes zoster while the rest of the family was having chickenpox. Fairly clear cut. The cortisone, in that child, was helpful; at least it allowed the child to sleep at night. I don't believe it prevented the development of his scars, certainly.

INDIRECT OPHTHALMOSCOPY

DR. TAYLOR SMITH of Boston discussed "Practical aids to ophthalmic technique: Indirect ophthalmoscopy," confining his remarks primarily to the binocular indirect ophthalmoscope developed by Dr. Schepens. He stressed the advantages of a brighter light, larger field, and a clearer, less distorted image, in addition to the advantages of binocular vision. Excellent colored drawings of fundus lesions were used to illustrate the talk.

Discussion. Dr. Frederick Verhoeff commented on his experience in using the reflecting indirect ophthalmoscope and emphasized its help in examining the fundi of high myopes. He was intrigued by the illustrations of lesions in the peripheral retina and said he would like to see them correlated with microscopic sections.

OPTICAL INSTRUMENTS USED IN OPHTHALMOLOGY

F. WACHENDORF (D.Eng.) discussed some of the defects of present-day ophthalmoscopes, slitlamps, and fundus cameras.

He briefly discussed some experimental work and calculations he is doing in an effort to improve these instruments.

ORBITAL CHOLESTEOTOMA

DR. LAWRENCE R. DAME of Pittsfield and DR. BENJAMIN ALPERT of Springfield reported a case which occurred in a 45-year-old man. The tumor caused exophthalmos and diplopia over a period of six months and was removed from the orbit by a trans-frontal approach. The diagnosis was confirmed by several pathologists.

CARDIAC RESUSCITATION

DR. J. GORDON SCANNELL, a surgeon, and DR. BERNARD D. BRIGGS, an anesthetist, both of Boston, discussed "Cardiac resuscitation in the anesthetic emergency of cardiac ar-

rest," and the measures to be taken if it occurs.

Dr. Briggs stressed the importance of prompt recognition of the problem, getting the patient in a favorable position for resuscitation, establishing a patent airway, and the means for oxygenating the blood.

Dr. Scannell described the technique of emergency thoracotomy and the technique of manually re-establishing heart action. If the heart does not respond, the cause may be ventricular fibrillation. Defibrillation can be achieved by using an electric current.

Discussion. Dr. Alson E. Braley of Iowa City commented on his personal experience with three cases. He said the chest incision can be done with a cataract knife.

Henry Adams Mosher,
Recorder.

OPHTHALMIC MINIATURE

In May 1751, the only child of a wealthy Clothier here (in Limerick) was playing with other children, in a Shoe-makers Shop; and taking up, a small cutting knife, it by some accident struck into the ball of the eye. It pervaded the anterior part of the Sclerotica, part of the Cornea Lucida, wounded the Foramen of the Iris, and the Chrystalin Lens. Being immediately sent for to prevent an inflammation, I blooded her; and as the wound was large I was apprehensive that the Humours of the Eye, might pass thro' the aperture, to prevent which I had a thin Plate of Lead beat concave, and holes made at its two sides: the concavity was to answer the Convexity of the eye, and the holes to have tapes in them, to fasten round the head. The dressings were, a little Saffron, infused in warm milk, to which was added, a small quantity of brandy. With this the eye was bathed morning and evening, and fine linen compresses wet in it, and applied under the leaden compress: the child was confined to her bed, and the next morning, took a lenient cathartick, and was ordered a low attemperating Diet. Tho' the Chrystalin, thro' the pupilla seemed clear, yet I assured them, the child would have a Cataract, which they did not attend to. In a few days the wound healed, without any material symptom, except, the ousing out, of a thin filamentous substance, which by the use of a little powder, made of a refined sugar, and Roch Allum, was soon destroyed—the child remained well ever since, but the Opacity of the Chrystalin is visible.

Mr. O'Halloran, Limerick, 1750,

A Critical Analysis of the New Operation for Cataract.

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EDITORIAL STAFF

DERRICK VAIL, *Editor-in-Chief*
700 North Michigan Avenue, Chicago 11
LAWRENCE T. POST, *Consulting Editor*
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BERNARD BECKER
640 South Kingshighway, Saint Louis 10
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VIRAL KERATOCONJUNCTIVITIS

The article on epidemic keratoconjunctivitis by Dr. Thomas A. Cockburn and co-workers in this issue of THE JOURNAL, and a second article by Dr. Cockburn to appear next month on a new type of keratoconjunctivitis presumed to be viral, accentuate the growing importance of viruses in external ocular disease. The interest of the United States Public Health Service in keratoconjunctivitis will be a most welcome aid to

ophthalmologists in their efforts to elucidate the problems still remaining in etiology, epidemiology, and therapy.

Although much work remains to be done on the problem of etiology, it is now known that at least seven different types of viral keratoconjunctivitis or conjunctivitis can be differentiated, either on the basis of clinical signs and symptoms or on laboratory findings.

The first of these seven types, *trachoma*,

although steadily decreasing in incidence in the United States, remains the eye disease problem of greatest worldwide importance.

The second type, *inclusion conjunctivitis*, has also been showing a marked decrease in incidence, due no doubt to the widespread use of sulfonamides and the broad spectrum antibiotics on the primary genitourinary disease.

The third type, *acute follicular conjunctivitis*, *Beal*, is occasionally seen in the United States but has only limited importance because of its short duration and the absence of corneal changes. Its occurrence predominantly in the summer and in connection with swimming pools makes it one of the three types of viral conjunctivitis known to be transmitted to swimmers.

The fourth type, *Newcastle disease conjunctivitis*, is caused by a well-defined virus and is transmitted from fowls to man, especially among packing-house workers. By virtue of its short duration and the absence of corneal complications, however, it too has only minor significance.

The fifth type, *epidemic keratoconjunctivitis*, on the other hand, has become of major interest to ophthalmologists, and particularly to those unfortunate enough to have had office transmissions. The high communicability of the disease and its transmission from patient to patient by means of contaminated fingers, solutions, and tonometers has made of it a sword of Damocles hanging over every ophthalmologic office. In spite of the epidemiologic data already accumulated, office transmissions, as indicated in Dr. Cockburn's paper, seem still to be occurring.

Although membranous forms leading to symblepharon have been noted on occasion, the early fears that permanent damage would result have evaporated. In spite of the lack of major corneal scarring, however, the disease is temporarily incapacitating and therefore of considerable economic importance. As an occupational disease of ophthalmologists, moreover, it ranks significantly; countless doctors and nurses contracted it during the 1941-42 and 1946 epidemics.

The sixth type of viral keratoconjunctivitis, caused by *herpes simplex virus*, though much less dramatic since it does not occur in epidemic form, is actually of far greater importance by virtue of the severe visual damage all too frequently entailed. Its emergence in the United States since the war as the most important cause of keratitis has resulted in part from the effective control of the bacterial types of keratoconjunctivitis by the sulfonamides and antibiotics, and in part from the greatly increased frequency of the disease for which no adequate explanation has as yet been offered.

In addition to increased frequency, greater severity has been noted in all sections of the country, and bilateral cases, which were formerly of extreme rarity, are now a common occurrence. Corneal perforations, previously unheard of in herpes simplex keratitis, have followed; these are probably due to the common use of cortisone, with its unfortunate masking effect, in the treatment of the disease.

The greatly increased frequency of the primary type of herpetic keratoconjunctivitis, whose conjunctival phase simulates epidemic keratoconjunctivitis, is of special interest and should be considered in the differential diagnosis of every case of suspected epidemic keratoconjunctivitis. Fortunately no instance of office transmission of the herpetic affection has been recorded.

The description of a seventh and apparently new type of keratoconjunctivitis by Dr. Cockburn calls attention to the possibility that other still undefined types of viral keratoconjunctivitis may exist. Epidemics of this "*Greeley type*" have been reported in Missouri, Utah, and California, in addition to the original epidemic in Colorado. The apparent transmission of this disease through swimming pools shows that the term "swimming pool conjunctivitis," originally applied to the adult form of inclusion conjunctivitis, is no longer suitable. The agent has not yet been isolated, but the occurrence of the disease in the late summer months, its predilection for children, the occasional neurologic features

which accompany it, and particularly the similarity of the pharyngeal signs to herpangina, suggested to the writer that it might be due to one of the Coxsackie viruses, but studies in connection with the two California epidemics failed to substantiate this possibility.

The increasing importance of viral keratoconjunctivitis, and particularly of the herpetic types, makes its study on a national scale a pressing need. The interest of Dr. Cockburn and other members of the United States Public Health Service Communicable Disease Center should be welcomed by the ophthalmologists and virologists working on these diseases all over the world.

Phillips Thygeson.

IN REGARD TO THE RIDLEY IMPLANT

About three months ago on a television program, and more recently by the newspapers, the public was informed of the Ridley implant in cataract surgery. Almost immediately ophthalmologists were contacted by patients eager for the new operation which would restore their sight without the use of glasses.

The operation is not as simple as that. In fact, there is great danger in the implanting of a foreign substance into the eye. By printed and verbal reports we are told that eyes, into which acrylic lenses have been implanted, remain irritated for a long period of time and must be kept quiet by the constant use of cortisone. Only a comparatively few eyes have been able to tolerate the foreign body. When cortisone is discontinued, inflammatory cells float in the anterior chamber, gather on the surface of the implant, and a beam is seen with the slitlamp. The iris becomes fibrotic, and connective tissue forms over the implant. What happens is well illustrated in the section of an eye sent to Dr. Derrick Vail by Mr. John Foster of Leeds, England, with the following history:

"The patient, a man, aged 28 years, was injured

in a football game about two years ago, and gradually developed a mature cataract, the other eye being normal. The cataract was extracted extracapsularly and a lenticulus was inserted. This was followed by a good deal of iritis, but it subsided with cortisone in about two and one-half weeks. The patient, who was afraid of losing his job, did not return again for six weeks, at the end of which time he was found to have hypopyon iritis. This was gradually subsiding, but in view of the other normal eye and the ultimate prospects of vision in the operated eye being rather poor, the eye was excised and sent to the pathologic institute for section. In order to cut the section, the lenticulus was dissolved out with chloroform."

Study of the section shows that the corneoscleral wound is well healed. The intratrabecular spaces are obstructed by migrated iris pigment epithelium. The iris is more or less densely infiltrated with cells of chronic inflammation, chiefly lymphocytes.

The pigment epithelium, especially on the side of the operative wound has disintegrated and migrated and, through the gap in this layer, inflammatory cells, connective tissue, and giant cells extend into the posterior chamber and form a dense band around the entire acrylic lens. This membrane is five to six cells in thickness and the foreign-body giant cells are numerous.

Only on one side is a segment of lens capsule in intimate contact with this connective tissue. The remaining lens remnants have no connection with it and form a Soemmering's ring posterior to it. The connective tissue membrane is in intimate contact with the posterior iris surface forming a pupillary membrane and retrodisplacing the roots of the iris.

The ciliary body, choroid, and retina show only a minimal cellular reaction without exudation into the vitreous.

The inflammatory reaction is confined to the iris and the connective-tissue membrane is an answer to the insult of the irritating acrylic lens. The implantation of any foreign body inside the eyeball is a very dangerous procedure as is well illustrated by this case report.

Georgiana D. Theobald.

XVII INTERNATIONAL CONGRESS OF OPHTHALMOLOGY

The International Council of Ophthalmology has extended the scope of the XVII International Congress of Ophthalmology scheduled to be held in New York in September, 1954. In addition to the program already arranged for the New York meeting there will be a two-day session in Montreal, Canada, on Friday and Saturday, September 10 and 11, 1954. The congress will reconvene in New York on Monday, September 13th, and continue through Friday, September 17th. The registration fee will cover both the Montreal and the New York sessions.

Details of the two meetings have not been fully developed and will be announced later. Preliminary announcements including forms for registration, for travel and hotel reservations, and for submitting contributions to the program have been mailed to all ophthalmologists in the world whose addresses have been obtained. These applications should be completed as soon as possible, particularly by those from overseas. Foreign guests who expect to attend both the Montreal and the New York sessions should apply NOW for a United States visa as well as a Canadian one.

Advance registration and the administrative affairs of the congress will be handled through the office of the secretary general, Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minnesota. There will, of course, be close liaison between the Canadian and the United States organizations.

The extension of the congress will add luster and importance to what already gives promise of being one of the most stimulating of international medical gatherings. It means that the ophthalmologists of Canada join those of the United States in acting as hosts to colleagues from all parts of the world.

CORRESPONDENCE

OPHTHALMOLOGY IN VILLAGE INDIA

Editor,
American Journal of Ophthalmology:

As I go back to India in a few days, to start my 30th year there, I want to share some observations on the Indian village ophthalmic scene with each one in the ophthalmic profession. It is of greater significance for you to share my earnest hope for reaching many thousands of the blind in Indian villages with the sight that it is the right and duty of the science of ophthalmology to give.

In India most of those who come to our hospital, and all of those whom we visit in the villages, have not seen an ophthalmologist previously. There are not enough ophthalmologists to meet the need: the blind with cataracts in India are blind simply because our science does not reach them.

A partial survey of the Central Provinces (now called Madhya Pradesh) indicated that one out of every hundred of the population had operable cataract. Conservatively, I would estimate that there are a million people with operable cataract in India. This is so in spite of the fact that it is estimated by Katik Chandra Dutt* that all the surgeons in India do 100,000 cataract operations a year! This count does not include the operations of the couchers, who still operate in India. The remainder, the million people blind with operable cataracts, are left without a chance of ever regaining their sight.

I will be happy if someone can correct me, but I believe that there is not more than one trained ophthalmologist for every million of the Indian people. According to Dr. Sorab N. Cooper, secretary of the All India Ophthalmological Society, Laude Mansions, Bombay 6, there are less than 300 members in the society. Dr. Cooper is the person with whom to get in touch for any information on ophthalmology in India. Not included among

*Katik Chandra Dutt: Arch. Ophth. 18:897 (Dec.) 1937. Quoted by Dr. Dutt in Arch. Ophth., 23:908 (May) 1940.

the 300 members of the All India Ophthalmological Society are some general surgeons who are doing ophthalmology in the course of their regular work. Some of these do acceptable surgery of the eye. In spite of this, the fact that the coucher is still able to practice, even in some of the great cities, gives one slight understanding of the immensity of the problem.

The four institutions with which I am personally familiar are the Christian Medical Colleges at Vellore in South India and at Ludhiana in East Punjab, the Christian Hospital at Miraj in Bombay State, and the Christian Hospital at Mungeli in the Central Provinces. These together do about 3,000 cataract operations a year. Other institutions, private and government, throughout India have done for many years (and continue to do) large amounts of surgery of the eye.

Eye surgery is carried on both in the hospitals and in the villages, for ophthalmic surgery lends itself particularly well to the mobile unit. A team of 12 to 14 persons, as a unit, can do a lot of surgery in two days. Our immediate effort is to try to increase the number of cataract operations to 10,000 per year in the four hospitals. Most of the increase will be through the utilization of mobile units, for there is no limit to the number of eyes available for operation when these units go to the villages by car and by truck. These units do not only cataract extractions but whatever ophthalmic surgery is necessary—plus the occasional emergency, such as an acute retention of the urine or a strangulated hernia.

Doctors who go to India have many of their finest experiences surgically, and personally, when they join with the hospital teams which go into the villages to operate. The ophthalmologist in India finds many compensations for his services, the greatest of which is the gratitude of his patients. Especially thankful are the deaf who, having been blinded with cataracts, are in contact with their surroundings only with the senses of touch, taste, and smell. Renewed sight

means much to them. One out of 20 of our patients is troublesomely deaf, and one out of 50 is absolutely deaf. What great satisfaction the surgeon has in giving such people their vision!

The patients who can thank us least are the little children. These youthful patients, transformed from blindness to anticipation of normal activity, go home to give parents and fellow villagers amazement and great joy. Five percent of our cataract patients are children.

Professionally, a doctor in India has a great opportunity for a varied and extensive practice of medical and surgical skills. One young ophthalmologist who came to India for about four months did more cataracts in his first day of surgery than he had done in the previous year in Europe.

The extremes to which many pathologic conditions are allowed to go before the patient will come to the hospital is characteristic of India. In glaucomatous eyes, tensions of 80 mm. Hg and above are not uncommon. Cases have been seen in which both eyes were blinded by pterygium.

Keratomalacia is most pathetic because it is so easily preventable. Infant after infant, child after child, and even an occasional adult, appear with the cornea lost from the lack of vitamin A and of fats. Keratomalacia can be cured with dramatic speed if treated in time. The fish scale cornea of prekeratomalacia will change to normal clearness within 14 hours after the injection of 50,000 units of vitamin A. What great good could be done for the children of India if they could have some of the 50,000,000 pounds of butter stored by our government!

We have done only a few corneal transplantations because of the difficulty in obtaining donor eyes. Muscle cases do not come to operation often as most of the people feel that crossed eyes is a light affliction and having it cured may open the way for something even more severe.

The routine operations are for glaucoma, for entropion and the other complications of

trachoma, and for cataract, as stated, the greatest cause of curable blindness in India. The operation for cataract is the most common eye operation done in Indian clinics. Happily, 98 percent of the patients who come to us with operable cataracts will, and do, see again.

I have been asked why there is so much cataract in India. The question cannot be answered completely. Research in this field, as in others, is needed. In India, along with the early development of presbyopia there appears to be an early development of cataract. People not only get cataracts earlier, they also die earlier in India than they do in America. The entire cycle of birth, life, old age, and death occurs in fewer years. Accurate comparison of ages between the people of the two countries is impossible. The simple, kindly Indian village people do not know their ages, and the ages that are listed on our hospital records are only our best estimates.

Ophthalmologists who have finished their work for the American Board examinations and candidates for the board certificate who are interested in the experience available in India can communicate with Dr. Edmund B. Spaeth, 1930 Chestnut Street, Philadelphia 3. Dr. Spaeth has been clearing the ophthalmologists who want to come to India to work with us.

If scholarships could be made available to American doctors for travel to India for such work, and to Indian doctors for study in this country, the benefit to all would be very great. I would appeal for such scholarships to any who are in a position to give this kind of help.

In addition to these travel scholarships—and because of them—funds for an increased volume of surgery would be needed. If a larger number of American surgeons came to India to do philanthropic work, or for personal study, this increase in funds would be needed so that the number of eye operations could be increased in order to give the visiting surgeon really worthwhile

surgical experience. We do not expect the volunteer surgeons to make financial contributions for they are contributing their services to the hospital.

It is this matter which is all important; contributions for the work must keep up with the expansion, otherwise the cause will fail and the blind continue blind. The minimum cost per operation is \$10.00.

Surpassing the personal professional gain possible in this work, however, is the fact that men, the former blind and their friends, love God and their fellow-men more as a result of it. The blind of India have a regard for those who have helped them that is very close to worship, little as it is deserved. Such gratitude is a measure of the need for medical work and is, in itself, a call to help.

(Signed) Victor Rambo,
Vellore, N.A., India.

BOOK REVIEWS

LE TRACHOME. By Roger Nataf. Paris, Masson et Cie, 1953. Preface by A. Cuénod. 426 pages, 46 figures, 16 color plates, bibliography, index. Price: 3,700 francs.

To those who are familiar with the literature on trachoma, the name of Nataf is most familiar. His preceptor, Cuénod, and he published a book of the same title in 1930 which had great influence on the students of this world-wide disease.

In 1933, Cuénod and Nataf began their work on the association of the inclusion bodies, discovered by Prowazek and Halberstaedter in 1907, with trachoma. Busacca, Thygeson, and other workers elsewhere were also working on this problem during this time.

The present volume is a complete study of the disease. It discusses the history, signs and symptoms, experimental studies, etiology, therapeutics, and prophylaxis. The illustrations are beautiful, the text clear and concise, and the bibliography most complete.

Although trachoma is fast disappearing from this country and many practicing oph-

thalmologists here have never seen a case of it, a knowledge of the disease is essential to all ophthalmologists. I promise that, after reading this book and studying the illustrations particularly, trachoma in a patient will be recognized at once.

Derrick Vail.

BULLETIN DE LA SOCIÉTÉ BELGE D'OPHTHALMOLOGIE. No. 100, February, 1952, and No. 101, June, 1952. Bruxelles, Imprimerie Medicale et Scientifique 67, Rue de l'Orient.

The February, 1952, *Transactions* of the Belgian Ophthalmological Society contains as its main contribution Jean Michiels' paper on the therapeutic value of antibiotics in ophthalmology with the exclusion of penicillin. This comprehensive review constitutes a continuation of the report on sulfonamides and penicillin, given by De Jaeger and Weekers before the same society in January, 1946.

The report discusses the chemical, biologic, and pharmacologic properties, and the clinical results on extraocular and ocular lesions of streptomycin, aureomycin, terramycin, chloromycetin, and other more or less effective antibiotics. It also contains a description of their modes of application, hazards in their use, and toxic and allergic reactions. The synergistic and antagonistic action of the different antibiotics alone and in combination with other drugs is discussed at length, as well as the dangers of increasing the resistance of the offending organisms. The many tables, schematic and graphic presentations of the results and failures in the use of antibiotics makes easier an evaluation of their efficiency. The successful treatment of severe retrobulbar neuritis with aureomycin is especially emphasized.

The excellence of this paper was stressed by L. Weekers, R. Weekers, R. Wiball, A. Meunier, and G. P. Sourdille who called special attention to the importance of sensitivity tests of micro-organisms toward the different antibiotics.

Calmettes, Deodati, and Monnier believe aureomycin to be the most effective antibiotic in staphylococcal infections. They advise against combining it with penicillin. G. M. Bleeker reviews his research work on antibiotics.

P. Danis, M. Humblet, and P. Lambert report a case of retinal periphlebitis treated with streptomycin. They recognize a beneficial effect on the fresh inflammatory lesions. Vascular changes, recurrent hemorrhages, and strand formations in the vitreous were neither prevented nor favorably influenced by this treatment.

M. Humblet recommends the early use of streptomycin in tuberculous iridocyclitis and periphlebitis, either by intramuscular or subconjunctival injections or by a combination of both techniques. J. François presents an analysis of the uses of cortisone in ophthalmology.

The last paper of this session was read by Ch. Thomas, J. Cordier, and B. Algan. They regard a certain type of spontaneous luxation of the lens as part of a new syndrome, namely, the Ehlers-Danlos syndrome. This is a generalized disorder of the mesoderm and consists in a hyperelasticity of the subcutaneous tissues and the joints and a pronounced fragility of the skin. A congenital weakness of the zonula could well be a part of a systemic disease of this kind. The authors observed a 48-year-old man who presented all these signs and symptoms and also had a subluxated cloudy lens. In spite of an uneventful cataract extraction the wound did not show any tendency to heal and had to be repaired twice. Attention was called to the management and prognosis of surgery in similar cases.

The June, 1952, *Transactions* contains papers on a wide variety of subjects, the obituary on J. Van Der Hoeve, and the minutes of the meeting of the administrative section on June 29, 1952.

J. François and M. Rabaey report their studies with the phase-contrast microscope which until now has been rarely used in

ophthalmologic research. They recommend its use for the examination of the lens, corneal endothelium, and pigment epithelium. They also make suggestions for the examination of the corneal stroma by increasing the contrast in such a way as to make the collagen and mucoid part of the stroma selectively visible.

J. François and R. Moens discuss the basic principles and advantages of the electronic tonometer, Jules Zanen presents a new and practical method for the study of the central color fields.

M. Appelmans and P. Lelos review the history and give the modern concepts on systemic elastosis and complicating chorioretinal lesions. They stress the importance of a survey not only of the skin but also of the cardiovascular system and the intestinal tract whenever disturbances of this kind are suspected. Since this is a generalized disease of the elastic tissue, a full examination of Bowman's and Descemet's membranes, sclera, conjunctiva, synovial membranes, and basal membrane of the inner ear is recommended. Senile and other forms of degenerations of the macula occasionally are monosymptomatic cases of pseudoxanthoma elasticum. Generalized elastosis often is accompanied by a hypercholesteremia. Two cases are discussed in detail.

A. Meunier read an interesting paper on concomitant squint with diplopia. Sevrin and Collier draw attention to the disturbances of convergence in exophoria and discuss the most simple and most practical methods for handling those difficulties.

F. Roussel discusses the differential diagnosis of vertical diplopia. He describes the co-ordimeter of Hess-Lees and its use. He also comments on Franceschetti's procedures and their merits. He uses both methods but recommends the latter in especially complicated cases.

L. Alearts gives a statistical survey of the causes of blindness in Brussels for the last 14 years. In spite of the use of antibiotics, inflammatory diseases were the cause of

blindness in 21.06 percent of all cases. J. Sevrin and J. Lamrechts recommend five-percent pyribenzamine solution for allergic conjunctivitis.

J. François and J. P. Deweer review the etiology of tuberous sclerosis and give a detailed report of a case of their own. Special attention is paid to neurologic disturbances and electro-encephalography. Deviations and asymmetry in the occipital leads and paroxysms in the occipital leads, more pronounced in hyperventilation than in stroboscopy, were thought to be characteristic for this disease.

M. Appelmans and L. Heffinck recommend systemic cortisone treatment in retrobulbar neuritis; nevertheless, treatment based on cause should not be neglected. G. Mortier suggests fever therapy in retinopathy of malignant hypertension. P. Huwart discusses a new instrument for prevention of hemorrhage during enucleation.

M. Coppez and L. Coppez showed several motion pictures of cataract extractions and fistulating operations. R. Weekers showed two motion pictures of intracapsular cataract extraction, with Arruga's capsule forceps in one and with Harrington's erisophake in the other.

Alice R. Deutsch.

OPTIC-DIENCEPHALIC PHYSIOPATHOLOGY AND CLINICAL ASPECTS. By B. Alajmo and A. Rubino. Report to the XXXIX National Congress of the Italian Ophthalmological Society.

In 1948, the Italian Ophthalmological Society assigned to the authors the task of making a report on the physiopathologic and clinical relations between the eye and the diencephalon.

PART I (121 pages) presents brief embryologic and gross anatomic descriptions with details of the macroscopic topography and the nuclear architecture of the diencephalon. This is followed by a discussion of the direct optic-hypothalamic nerve pathways and the indirect ones. Finally, the neuroveg-

etative system is reviewed under the headings of its metabolic, exocrine, endocrine, striate and smooth muscle, vegetative and neurosomatic functions, and hypophyseal regulatory centers. The first part is appropriately closed with Pende's comprehensive definition of the diencephalon, "the tropho-psycho-regulatory center," which serves as the meeting place of the neurochemical processes of the soma and psyche.

PART II (208 pages) discusses the physiology and physiopathology of the optic-diencephalon:

1. *The pupil.* Animal and human experiments concerned with the hypothalamic role in pupillomotor functions are reviewed. In the hypothalamus, which some consider to be the center of the activity of the sympathetic nervous system, two separate components concerned with pupillary dilatation have been demonstrated. One is sympatho-excitatory and the other is parasympatho-inhibitory. Pupillary reactions to pain, light, and accommodation have their pathways traced and modus operandi explained on the basis of either one or the other and even both mechanisms. Thus all pupillary functions are under the influence of the hypothalamus.

2. *Ocular tension.* Some authors believe they have localized a center for the regulation of intraocular pressure, the lateral part of which has a sympathetic action and elevates the tension, while the central part lowers the tension through parasympathetic activity. Illumination of one eye reduces the tension of the fellow eye kept in the dark, which rises after exposure to light. This reflex is mediated centripetally by retino-vegetative fibers along the optic nerve to the anterior portion of the diencephalon. The exact centrifugal course is not well understood.

A similar action on the pressure of the retinal arteries is referable to the diencephalon.

3. *Ocular vasomotor* response parallels that of the intraocular pressure.

4. *Visual function.* The metabolism of photosensitive substances is believed regulated by centrifugal fibers from the external geniculate body. Dark adaptation is more rapid when measured at night and slower during the day time. The authors attribute this difference to the diurnal rhythm of metabolic, hormonal, and neurovegetative functions.

The threshold of excitability of the peripheral retina (rods) is raised by a "block" centrally. The diencephalic influence thus is concerned only with the peripheral retinal elements, the rods, as with dark adaptation, also a rod function. No understood influence on color vision can be reported.

5. *Opticohypothalamic reflexes.* Under the photomelanophore reflex, the well-known change in the color of various animals when exposed to different colors is explained by the effect of light stimulus to retina via the optic pathways to the supraoptic nucleus, hypophyseal peduncle, and the pituitary gland. As an example of the photogonadotropic reflex, the well-known increase in egg laying by hens after exposure to artificial illumination is given. The exact mechanism by which the photoglycemic reflex affects glycemia is not known, but it appears that involved are the secretion of pituitary, pancreatic, and suprarenal hormones. Under opticogastro-motor and opticopresso reflexes the authors point out that stimulation of the retina with light produces increased gastric motility. It also causes changes in the amplitude of oscillations of the arterial pressure and pulse rate which vary with white and different monochromatic light.

Besides these opticohypothalamic reflexes, there are other well-known diurnal variations in many hormonal and vegetative functions. At night there occurs a drop in temperature and of blood-sugar; nails and hair grow faster; spontaneous estrus occurs in some animals only at night; suprarenal activity is lowered at night; melanophore hormones in pituitary and blood increase at night.

PART III (187 pages, 34 figures) is con-

cerned with the pathology and clinical aspects of the subject and discusses disturbances of the pupillary reflex, tapetoretinal degenerations, and glaucoma. Under glaucoma, the authors note that there is a lowering of the light-sense threshold in early glaucoma without acuity changes, field changes, or even a rise in tension. Changes are demonstrable in the photoglycemia reflex curves. All these findings point to central diencephalo-hypophyseal disturbances in glaucoma.

J. J. Lo-Presti.

ARQUIVOS DO INSTITUTO PENIDO BURNIER.
Campinas, Brazil, 1952, v. 9. Clothbound,
198 pages.

The first 16 pages are dedicated to official speeches delivered at the meeting of the institute on June 1, 1952.

Lech Junior discusses the concept of blindness, which he divides into four categories: (1) total blindness; (2) practical blindness, in which there is not enough vision for a lucrative occupation; (3) occupational blindness, in which the individual is unable to pursue his current occupation but can be trained for another; and (4) educational blindness which prevents students from receiving education through the usual ways of teaching. Evaluation of blindness is based on an estimation of visual acuity with Snellen's test types, the visual field, and binocular co-ordination.

Martins Rocha points out that the difficulty in making a diagnosis of mycoses in ophthalmology must be ascribed to technical difficulties in laboratories. The ophthalmologist is especially interested in primary mycoses, those in which, at least at the begin-

ning, one structure of the eye alone is invaded. He describes in detail the many mycoses affecting lids, conjunctiva, cornea, lacrimal apparatus, retina and choroid. Many of these are very rare. He reviews briefly the world literature and especially all Brazilian cases published and refers in detail to seven cases of mycosis which he has studied. He emphasizes that in all cases of endocular mycosis a confusion with lues or tuberculosis is possible.

Monteiro Sales classifies the ocular mycoses. The English-American classification in which moldlike and yeastlike fungi are recognized is unacceptable in Brazil, because both words have the same meaning in Portuguese. The botanic classification is useless for the clinician because the pathogenic species are very few. He follows Willis in classifying mycoses by their localization—as mycetomas, tegumentary mycoses, intraocular mycoses, and canalicular mycoses. The details and subclassifications of each one of these groups are given.

Geraldo Paletta reports about a case of chalcosis and Souza Queiroz describes a case of scleral staphyloma and retinal detachment.

Roberto Barbosa discusses the normal and pathologic vitreous and reports several cases of asteroid bodies.

J. Penido Burnier discusses Hurler's disease, which, he thinks, is one of the lipoidoses. The chemical nature and the localization of the lipid deposits distinguish the various diseases in this group.

A brief summary of the 71 clinical sessions held at the Institute from 1949 to 1951 occupies the last 80 pages.

Walter Mayer.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

- | | |
|--|--|
| 1. Anatomy, embryology, and comparative ophthalmology | 10. Crystalline lens |
| 2. General pathology, bacteriology, immunology | 11. Retina and vitreous |
| 3. Vegetative physiology, biochemistry, pharmacology, toxicology | 12. Optic nerve and chiasm |
| 4. Physiologic optics, refraction, color vision | 13. Neuro-ophthalmology |
| 5. Diagnosis and therapy | 14. Eyeball, orbit, sinuses |
| 6. Ocular motility | 15. Eyelids, lacrimal apparatus |
| 7. Conjunctiva, cornea, sclera | 16. Tumors |
| 8. Uvea, sympathetic disease, aqueous | 17. Injuries |
| 9. Glaucoma and ocular tension | 18. Systemic disease and parasites |
| | 19. Congenital deformities, heredity |
| | 20. Hygiene, sociology, education, and history |

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Akiya, H. **Mitochondrial substance in the visual cell.** *Acta Soc. Ophth. Japan* 57:359-364, June, 1953.

A histochemical study of the chemical structure of the visual cells in animals similar to Akiya's previous one (*Ibid.* 56:767, Aug., 1952) revealed that the middle segments of the visual cells are stained by Heidenhein's iron hematoxylin and by Janus green and show a granular structure. This segment is positive for oxydase reaction and may be considered to consist of mitochondrial substance. The outer segment, on the contrary, does not stain with Janus green, although it is stained by iron hematoxylin which suggests that this segment has a nature like secretory granules. Yukihiro Mitsui.

Ascher, K. W. **Aqueous veins.** *A.M.A. Arch. Ophth.* 49:438-451, April, 1953.

The related literature is reviewed.

G. S. Tyner.

Kikkawa, Y. **The micellar structure of the cornea.** *Acta Soc. Ophth. Japan* 57:352-359, June, 1953.

The rabbit cornea was studied by

means of a polarising microscope. Optically, corneal fibers are a biaxial and negative crystal. The Y- and the Z-axis lie in the tangential plane to the cornea; the former is in the direction of the fiber and the latter perpendicular to it. The X-axis is in the direction perpendicular to the tangential plane. This relationship can well be observed in the periphery of the cornea, where the fibers are regularly arranged in a radiating direction. At the center of the cornea, where the arrangement of the corneal fibers is extremely irregular, the cornea apparently is uniaxial and negative. When the fiber is stretched the Z-axis rotates through 90°. In the light of these experiments the author discusses the micellar structure of the cornea. Yukihiro Mitsui.

Surgiura, S. **X-ray diffraction of the vitreous.** *Acta Soc. Ophth. Japan* 57:336-374, June, 1953.

The vitreous of cattle eyes was filtered through a glass filter. The residue was studied by X-ray diffraction as recommended by Debye-Scherrer, employing parallel Cu K α radiation. The pattern was then comparatively studied with that obtained in the rabbit cornea. Vitreous and cornea have some interference lines and

their periodicities are: 4.01, 2.91 and 2.23 Å in the vitreous, and 4.01, 2.91 and 2.22 Å in the cornea. The author considers, therefore, that the vitreous and the cornea have similar chemical structure. After an analysis of these lines he concludes that the vitreous and the cornea have a fringy micellous structure as they have crystalline and amorphous substances.

Yukihiko Mitsui.

Yamamoto, T. **Phase microscopic study of rabbit cornea.** *Acta Soc. Ophth. Japan* 57:262-264, May, and 296-299, June, 1953.

Unstained, frozen sections of rabbit cornea and lamellar sections of raw cornea were examined by phase microscopy. A membrane similar to Bowman's membrane is recognizable, which has been considered to be absent in rabbits by ordinary examinations. When a 0.5-percent solution of silver nitrate is instilled into the rabbit's conjunctival sac an edema of the superficial layer of the cornea is brought about which reaches its climax in two hours and disappears in 72 hours.

Yukihiko Mitsui.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Malatesta, C. **Histochemical study of the retinal phosphatase.** *Boll. d'ocul.* 32: 101-106, Feb., 1953.

Bulbs of albino rabbits were enucleated and immediately fixed in ice-cooled acetone. After 12 hours the lenses were extracted through a limbal incision and the bulbs were subjected to further fixation for 12 hours more in the refrigerator. Then, acetone at room temperature, followed by benzol, and paraffin of 56° were used for embedding and 4 to 5 micra sections were obtained and exposed for two hours to a temperature of 37° in a solution of CaCl_2 (anhydr.) 2 percent; MgCl_2 0.4 percent; glycerophosphate of sodium,

0.84 percent; sodium veronal 2.4 percent with a few drops of chloroform. After short washing in CaCl_2 , 1-percent solution, the sections successively passed through a 2-percent cobalt nitrate solution for 2 minutes, a diluted ammonium sulfate solution for one minute, washing in tap water 1 to 2 minutes, and contrast staining of the nuclei with carmine, and were mounted after passing through alcohol and xylol. Almost all of the retinal layers showed a definite phosphatase activity as shown in colored drawings of the nerve fiber layer, and the inner and outer granular layer; contrariwise, the pigment epithelium cells and the cones and rods showed none. (references)

K. W. Ascher.

Miyake, S. **Acid-fast bacteria isolated from the conjunctival sac.** *Acta Soc. Ophth. Japan* 57:335-345, June, 1953.

Miyake isolated five strains of acid-fast bacteria from the conjunctival sac, and studied their biological properties. They were not pathogenic when inoculated into rabbit vitreous.

Yukihiko Mitsui.

Nakayama, H. **Tuberculous allergy of the eye.** *Acta Soc. Ophth. Japan* 57:327-335, June, 1953.

In the first part of this essay the author summarizes his previous report on Koch's phenomenon in animal conjunctiva sensitized with B.C.G; in the second part, he evaluates the tuberculin reaction in the conjunctiva. He states that in guinea pigs a tuberculin reaction occurs very poorly, unless a high concentration of tuberculin (1 in 10 dilution) is used. Hyperemia and round cell infiltration are the changes brought about in the conjunctiva after tuberculin injection and there is little of the edema and swelling of connective tissue which is usually seen in the skin.

Yukihiko Mitsui.

Ovary, Z., and D'Ermo, F. **Quantitative study of the antibodies of the aqueous humor using a new biologic titer method.** *Boll. d'ocul.* **32**:69-73, Feb., 1953.

Ovary's new biologic method of antibody titration permits, in an accurate, quick and simple way, the detection of 0.003 gamma of antibody nitrogen of the egg albumin-anti egg albumin system. Using this method, the authors compared the blood titer with the aqueous humor titer of rabbits sensitized against chicken egg albumin. The fluids were intradermally injected into the abdominal wall of guinea pigs of about 250 grams; four hours later, 0.5 cc. of a 2-percent solution of crystallized egg albumin with 0.5 cc. "Geigyblau 536" was injected per venam. Ten minutes later the animals were killed and the inner surface of the skin was evaluated for positive reaction (blue stain). The highest dilution capable of producing a positive reaction indicates the titer in "skin-sensitizing units" (Ovary) per 0.1 cc. of serum or aqueous. In the system investigated, one unit corresponded to 0.003 gamma of nitrogen. The antibody content of the aqueous was found to be inferior to that of the serum (table), the relation varying from 1/10 to 1/350. In units, the highest aqueous humor titer was 100, the lowest 20.

K. W. Ascher.

Ryan, H., and Plaisted, S. **A method of mounting ophthalmic museum specimens in a solid medium.** *M. J. Australia* **1**:776-777, May 30, 1953.

The authors describe in detail a method of mounting ophthalmic specimens in gelatine combined with "Formit" resin enclosed in Petri dishes. A stained section can be mounted alongside the specimen. Considerable detail can be seen in the section by means of a hand lens and different aspects can be compared. The solid medium allows repeated handling without damage. Ronald Lowe.

3

VEGETATIVE PHYSIOLOGY, BIO-CHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Alagna, G. **Isoniazid in ophthalmology.** *Arch. di ottal.* **57**:5-16, Jan.-Feb., 1953.

In experiments on rabbits, the author found that Isoniazid, administered locally in drops or by subconjunctival injection penetrates into the aqueous and rapidly reaches therapeutic levels. Intramuscular injections of larger than therapeutic doses can occasionally cause congestion and hemorrhages in the iris and the ciliary body. Isoniazid provides a well-marked, but not absolute, protection against experimental infection with tuberculosis. It does not influence the repair of experimental corneal lesions but hastens the disappearance of corneal vascularization and opacities. In man, administration of high doses slightly lowers the blood-aqueous barrier. John J. Stern.

Alajmo, A., and Ambrosio, A. **Results of experimental administration of streptokinase-streptodornase in ophthalmology (second part).** *Arch. di ottal.* **57**:25-33, Jan.-Feb., 1953.

Subconjunctival or retrobulbar injection of streptokinase-streptodornase in rabbits with hyphema or intravitreal hemorrhage is well tolerated but without effect on the absorption of the blood. Injections of small doses into the anterior chamber or the vitreous are well tolerated but ineffective. Larger doses are followed by violent reactions with opacification of cornea and vitreous. In one patient, injection of the preparation into a subconjunctival hemorrhage failed to hasten absorption. In two cases of lid abscess injection with streptokinase-streptodornase was followed by marked improvement.

John J. Stern.

Alvaro, Moacyr E. **Sulphydryl in the treatment of corneal afflictions.** *Rev. brasil oftal.* 10:59-63, Dec., 1953.

The author reviews the theoretical physiologic basis for the use of sulphydryl (Hydrosulphosol) in corneal diseases. He reports good results specifically in corneal burns, chronic corneal ulcers and certain cases of chronic conjunctivitis.

Theodore Bisland.

Carta, R., and Cadeddu, N. **Device for collection of tears for lysozyme determination.** *Boll. d'ocul.* 32:87-90, Feb., 1953.

Photographs show the filter paper strips inserted under the lid of human and rabbit eyes; "Schleicher-Schuell 5893" are best suited. Thirty to 60 mg. of lacrimal fluid is collected, weighed on a precision scale, and the paper strip washed with buffer Walpole pH 6.25 which permits 100 percent recovery of the lysozyme. The amount of enzyme is estimated nephelometrically using Caselli's method. Logarithmic graphs demonstrate the lysozyme values ascertained.

K. W. Ascher.

Fanta, H., and Mayer-Obiditch, I. **The pathology of the optic nerve in acute methyl alcohol poisoning.** *Klin. Monatsbl. f. Augenh.* 122:388-394, 1953.

Rabbits were fed with food containing methyl alcohol. When symptoms of poisoning appeared several organs were removed under ether anesthesia. Histologic examination of the optic nerves revealed deposition of an acidophilic material into the sheaths and the perivascular connective tissue of the nerve. Various staining methods and fluorescence microscopy showed that this material was a protein. Similar changes were found in other organs. The basic pathologic process is thought to be a serous inflammation. (3 figures, 9 references)

Frederick C. Blodi.

Grosz, I., and Kedvessy, G. **Standardized eye ointments and drops.** *Klinica Oczna* 22:369-375, 1952.

The authors prepared vehicles for ointments which have proper pharmacological effect and at the same time spread well over the surface of the conjunctiva and mix well with tears. One mixture containing water and the other without it serve well for most of the usual types of medication.

Sylvan Brandon.

Harley, R.D. **Treatment of chemical burns of the eye.** *A.M.A. Arch. Ophth.* 49:413-418, April, 1953.

Calsulphydryl (hydrosulphosol) was shown to have no beneficial effect in the treatment of chemical burns of the rabbit cornea produced by a wide variety of agents.

G. S. Tyner.

Ichikawa, K. **Mode of wound healing in the cornea, a histochemical study.** *Acta Soc. Ophth. Japan* 57:374-389, June, 1953.

A sterile, standard injury was made in the cornea of guinea pigs with a trephine. The process of wound healing was studied, especially by histochemical analysis. The first step of healing is a regeneration of epithelium. The second step is a wandering of granular cells from the subconjunctival limbus into the proper substance of the cornea at the site of the wound. The granular cells burst forth at the wound border and the granules enter the new-grown epithelium. The granular cells seem to be mast cells. The granules are positive for the polysaccharide staining of Hotchkiss and for ninhydrin reaction. They show a metachromasia by toluidine blue and thionine stain. Ichikawa considers the granule to contain heparin. The granules stain with pyronine but do not stain with it after a treatment with ribonuclease or with hydrochloric acid. They have an absorption spectrum at the wave length of 2573 Å. The granules, therefore, also contain ribo-

nucleic acid. They do not contain glycogen. Yukihiro Mitsui.

Inami, E. **Vitamin B₁ in the retina.** Acta Soc. Ophth. Japan 57:346-349, June, 1953.

Vitamin B₁ in the animal retina was studied in sections by the thiochrome method and the fluorescence microscope. The vitamin is mainly found in the visual cells and plexiform layers of the retina and in the choroid in the form of co-carboxylase. Systemic administration of the vitamin results in an increase of it in the eye, in the portions mentioned above in particular. Hyaluronidase causes a reduction of it in the eye. In the developing chick embryo, the vitamin first appears in the choroid and in the retina by the ninth and the thirteenth day of incubation respectively. Yukihiro Mitsui.

Kozima, K., Ikema, M., Nagaya, Y., and Mazima, Y. **Phosphatase of the retina.** Acta Soc. Ophth. Japan 57:269-283, May, 1953, and Kozima, K., Nagaya, Y., Sano, K., and Mazima, Y. **Phosphatase of chick-embryo eye.** Acta Soc. Ophth. Japan 57:302-311, June, 1953.

In the first report, the authors studied the phosphatase of the retina histochemically in the eyes of man, cattle, dog, cat, rabbit, chicken and frog. They first describe the distribution of alkali- and acid phosphatase in the retina, and discuss the difference in the distribution of these substances among the animals. Ciaccio's fixative is recommended for the study. The light-adapted eye seems to have a little more acid-phosphatase than the dark-adapted. Nucleic acid-, ribonucleic acid- and desoxy-ribonucleic acid-phosphatase are found in nuclear layers. In the second report, the authors describe the developmental course of phosphatase in eye of the chick. Yukihiro Mitsui.

Krwawicz, T., Seidler Dymitrowska, M., and Vorbrodt, A. **Changes in distribution of the reduced form of vitamin C**

in the pathologically changed cornea. Klinika Oczna 22:301-307, 1952.

Vitamin C can be made visible by appropriate histochemical methods. Normally the greatest accumulation of vitamin C is in Bowman's membrane, under it and in Descemet's membrane. The authors examined 20 pathologically changed corneas; 7 in eyes with corneal degenerations, 3 absolute glaucoma, 8 corneal scars, 1 phthisis bulbi and 1 rupture of the sclera. In corneal degeneration intracellular vitamin C had decreased in the epithelium, but was present in the intercellular spaces; there were accumulations of it near the surface and a general decrease in all other layers. When Bowman's membrane was destroyed, vitamin C was accumulated under the epithelium, which did not stain for vitamin C at all. Corneal scars presented similar distributions of vitamin C, except that the superficial layers of epithelium showed uneven staining for vitamin C. In absolute glaucoma there is a general loss of the reduced form in the epithelium. In phthisis bulbi no vitamin C was present in the cornea. Sylvan Brandon.

Marconcini, E. **Methyl alcohol and hydrogen peroxide: their action on the optic nerve.** Arch. di ottal. 57:41-48, Jan.-Feb., 1953.

The toxic action of methyl alcohol is probably due to oxidative phenomena. The author treated rabbits poisoned with methyl alcohol by subconjunctival injections of hydrogen peroxide (1 cc. of a 1-percent solution). In two treated animals the histologic changes in the optic nerve were less evident than in two untreated animals. John J. Stern.

Martin, G., and Dor, E. **Early local signs of intolerance to cortisone.** Ann. d'ocul. 186:170-172, Feb., 1953.

A speedy reaction of the corneal epithelium occurred in three patients after

the use of cortisone and cleared immediately when the drug was discontinued. In the first patient the acute signs of a low-grade tuberculous interstitial keratitis had healed with heliotherapy. After one month of cortisone ointment there was an intense swelling of the corneal epithelium. In the second patient corneal desquamation came on within a few hours after a second subconjunctival injection of cortisone. The third patient, with a probable tuberculous uveitis, had had eight retrobulbar injections without incident, but after the fifth subconjunctival injection a severe reaction with pain, photophobia and ulceration developed.

B. T. Haessler.

McDonald, P. R., Leopold, I. H., Vogel, A. W., and Mulberger, R. D. **Hydrocortisone (compound F) in ophthalmology.** A.M.A. Arch. Ophth. 49:400-412, April, 1953.

Cortisone and hydrocortisone appear to have somewhat similar actions when applied topically to the eye. Hydrocortisone may be more potent in some respects than cortisone. Hydrocortisone proved to be effective in some cases where cortisone had failed (e.g. cortisone-resistant cases of uveitis, vernal conjunctivitis, and corneal ulcer). Both compounds have about the same inhibitory effect on fibrous tissue proliferation. Cortisone may be more effective than hydrocortisone in inhibiting corneal vascularization.

G. S. Tyner.

Salvi, G. L. **Action of metals on the in-vitro effect of penicillin.** Boll. d'ocul. 32: 91-100, Feb., 1953.

In usual therapeutic doses, sulfate of zinc and of copper inhibit the antibiotic effect of penicillin in vitro; in high dilution, however, (1:100,000) they increase the antibiotic action. Under the same experimental conditions, argyrol, protargol, mercurochrome, and the iodides of potassium, sodium and rubidium did not

alter the bactericidal activity of penicillin. (3 tables, references) K. W. Ascher.

Segal, P., and Berger, S. **Influence of alcohol on the efficiency of the eye and on the blood level of the vitamin A and carotene.** Klinika Oczna 22:283-290, 1952.

Visual acuity in bright and dim light, progress of adaptation to darkness, and the blood level of vitamin A and carotene were measured after the ingestion of ethyl alcohol by six healthy subjects 24 to 28 years of age. In the majority of cases there was a marked temporary lowering of adaptation; occasionally there was an improvement. Ingestion of alcohol did not influence the visual acuity or the visual field. The maximum effect of the alcohol occurred in one to two hours after ingestion. In the majority there was an increase of vitamin A in the blood.

Sylvan Brandon.

Yokoyama, M. **Oculovascular reflex.** Acta Soc. Ophth. Japan 57:285-287, June, 1953.

When low (0-13°C) or high (42-60°C) temperatures were applied to the conjunctival sac of rabbits under general anesthesia for ten seconds to five minutes an increase in blood pressure was brought about after an incubation period of about ten seconds. The degree of increase in blood pressure was proportional to the strength of the irritation but not to its duration. Beside the change in blood-pressure an inconstant change was brought about in pulse rate, respiration, and body motion. Yukihiro Mitsui.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Brown, K. T. **Factors affecting differences in apparent size between opposite halves of a visual meridian.** J. Opt. Soc. Am. 53:464-465, June, 1953.

This is a new study of the partition

experiment first published by Kundt and Munsterberg. Here, a luminous line target had a movable divider and fixation point, so that by moving a convenient dial the subject could indicate his monocular judgment of two equal lengths. This target could be used with either eye, horizontal or vertical. It is the mean error in such partition experiments which determines individual differences in the curve of a horopter surface. In six subjects, the experiment indicated a horopter convex toward the observer. The two eyes are seldom perfectly symmetrical, and may vary in the type of partition. Vertical partition differences had been observed in the past, but Brown has discovered a tendency for such differences to change regularly with the passage of time. He believes this trend to be cerebral, and to affect only the vertical length judgment. He concludes that while corresponding points in the horizontal meridians of the two eyes are asymmetrical and cannot correspond to equal lengths in space, such correspondence as does exist is stable.

Paul W. Miles.

Eames, Thomas H. **Correspondence between visual acuity, refractive error, and the speed of visual perception.** *Brit. J. Ophthalm.* 37:312-313, May, 1953.

In a previous study, it was shown by the author that most patients exhibited an increase in speed of visual perception proportionate to the magnitude of refractive error that has been corrected; however, in some, especially myopes, there was a decrease in the speed of visual perception after correction. This study, made on school children between 6 and 17 years, confirms the findings of the earlier one. A high correlation was found between the speed of visual perception and visual acuity, both before and after correction of refraction in both hyperopes and myopes. Many myopes, however, exhibited a decrease in speed of visual perception at

near while wearing their correction, probably because many myopic children prefer reading at the myopic punctum proximum to accommodating.

Morris Kaplan.

Ehlers, H. **Clinical testing of visual acuity.** *A.M.A. Arch. Ophthalm.* 49:431-434, April, 1953.

In 100 tested persons, the norm for visual acuity conformed to a visual angle of 5 minutes as used in the Snellen test chart. In the untrained observer and in children, the use of large print in primary reading books is justified because even though the visual acuity is normal, the time necessary to recognize a letter of 10 minutes is 1/10 of that necessary to recognize a letter of 5 minutes. In testing the visual acuity of children, single test objects should be used to obtain the best acuity, because the sense of form is most easily recognized in an otherwise empty field. Persons with an amblyopic eye can often recognize the right correcting lens when placed in front of the amblyopic eye even though the visual acuity is very low and not improved by the lens. This can be ascribed to an unimpaired light sense which enables the patient to perceive the feeblest circles of diffusion on the retina.

G. S. Tyner.

Falkowska, Zofja. **Pilocarpine test in the examination of disturbances of accommodation.** *Klinika Oczna* 22:271-282, 1952.

The author examined the accommodation of 72 people before and after instillation of pilocarpine, by placing increasingly stronger lenses in front of the eyes which were focused at 5 M. until visual acuity was reduced to 5/60. By eliminating the influence of convergence, the remaining accommodation was only "cortical." Its amplitude was not affected by pilocarpine, the eye was just rendered nearsighted. On examining people with

disturbance of binocular vision it became evident that the ability to accommodate is influenced by cortical impulses. An increasing reaction to pilocarpine in the eye which is fatigued by work suggests the possibility that there may be cortical and peripheral components in the process of fatigue of the eye. Sylvan Brandon.

Honda, H. **Spacial summation of the retina, especially concerned with Kohlrausch's bend phenomenon.** *Acta Soc. Ophth. Japan* 56:519-524, July 1952, 56:1194-1198, Oct., 1952, and 57:364-367, June, 1953.

Ring objects were placed in an adapter. When a thin ring was used, the adaptation occurred gradually and the final limen was high. When discs were used instead of rings, the results were similar with smaller discs. In both cases, however, the Kohlrausch's bend appeared at the definite time point. Discs of various size were used in prior light adaptation. When a larger disc of the same illumination was used, the rod section in the subsequent dark adaptation was protracted (in atropinized eyes), while little change was brought about in the cone section and the bend point. When a larger but darker disc was used in prior light adaptation, so as to make the product of the area of the disc and the intensity of illumination constant, the cone section of subsequent dark adaptation was steeper, the rod section less steep, and the bend point appeared in the earlier stage. The author further states that the bend can be observed even in a peripheral adaptation. Finally, he added some experiments in pathologic eyes and concludes that the bend phenomenon does not literally seem to be the transition point of rod and cone adaptation. Yukihiko Mitsui.

Knoll, H. A. **An infra-red skiascope and other infra-red ophthalmic research instruments.** *Am. J. Optometry* 30:346-350, July, 1953.

In the study of certain characteristics of the eye in various degrees of darkness, it is desirable to make measurements of refraction, pupil size, and accommodative state without exposing the eye to additional light. This could only be done by development of instruments using "invisible" light, which became possible during World War II with the infra-red converter image tubes. Such instruments include the skiascope, an objective optometer, a pupillometer, and an Purkinje-Sanson image viewer described by this author. Paul W. Miles.

Miles, W. R. **Effectiveness of red light on dark adaptation.** *J. Opt. Soc. Am.* 43:435-441, June, 1953.

Recent work seems to indicate that dark adaptation proceeds more rapidly under the influence of red light than it does under complete darkness. Cheshire in 1942 made such a claim in work which was confirmed by McLaughlin. Smith and Dimmick, in 1953, found no difference in red light and in complete darkness, while Miles in the present study found that 30 minutes use of a red goggle achieved a high degree of dark adaptation, but not so great as 30 minutes of complete darkness. The original observers used slightly different conditions, and said that dark adaptation was more rapid under red light 10 minutes and darkness 10 minutes than it was under darkness for 20 minutes.

Paul W. Miles.

Neumueller, J. **Optical, physiological and perceptual factors influencing the ophthalmometric findings.** *Am. J. Optometry* 30:281-291, June, 1953.

Ophthalmometer (or keratometer) readings differ from the correcting cylinder power because of the difference of 13.75 millimeters in the distance of the cornea and the correcting lens from the far point of the eye. However, the difference in power depends also on the spheri-

cal ametropia being corrected at the same time. For instance, if the ophthalmometer reads 6.00 diopters of astigmatism, and the spherical ametropia is -8.00 diopters, the correcting cylinder would have to be -8.14 diopters. If the spherical ametropia is $+18.00$ diopters, the cylinder correcting 6.00 diopters of corneal astigmatism would have to be only -3.62 diopters. The effect of unequal or oblique cylinders before the eyes on perception of a room is discussed briefly. Paul W. Miles.

Pestrecov, K. **Visual tasks in aerial mapping with multiplex equipment.** *Am. J. Optometry* 30:366-373, July, 1953.

A high degree of stereoscopic acuity is required for mapping from aerial photography. A system of red green anaglyphs is used, in which for best results the green filter includes -0.25 diopter sphere. Since the work is under intermittent threshold conditions, there is complaint of fatigue and eye strain. There has been no proof of any eye damage, however, and the complaints are considered psychological.

Paul W. Miles.

Rzymkowski, J. **Stereophotographic and stereophotogrammetric reproduction of the sclera of the living eye by the method of Dencks-Rzymkowski.** *Photog. u. Wissensch.* 2:1-8, 1953.

An elegant method for the haptic fitting of contact glasses is described which makes troublesome Negocol molds superfluous without anesthetizing the eye. The pair of stereograph pictures made by a flashlight exposure is analyzed photogrammetrically and the resulting curves are used in the selection or construction of a contact glass. F. H. Haessler.

Sloan, L. L., and Altman, A. **Aniseikonia and the Howard-Dolman test.** *J. Opt. Soc. Am.* 43:473-478, June, 1953.

In his original description, Howard found several subjects who persistently

set one rod a precise amount nearer than the other for subjective equality. This type of error was shown to be due to aniseikonia in 1944 by the Rowlands. The present work determined the effect on settings of the Howard-Dolman two-rod test of aniseikonic magnifying lenses before one eye. The results showed a definite but unpredictable amount of near error of the rod homolateral to the magnifier. Large amounts of aniseikonia interfere with the Howard-Dolman test by reducing stereopsis. It was shown by Ames and Ogle that the most sensitive two-line test for aniseikonia required fine strings, not ropes or rods, so that the Howard-Dolman test is not suitable for aniseikonia screening as suggested by Hirsch. Tests for stereoscopic acuity by a two rod test should measure the variation about a mean position, not a comparison of relative rod distances.

Paul W. Miles.

Starkiewicz, Witold. **Visual acuity as a measure of impairment of the eye.** *Klinika Oczna* 22:323-338, 1952.

This is the first half of a paper on visual acuity. The author discusses in detail the physiological background of visual acuity, considering the size of the image on the retina and all the elements influencing its sharpness. A number of optical formulas are presented. Sylvan Brandon.

Sterling, W. **The specification of color of ophthalmic glasses.** *Am. J. Optometry* 30:335-345, July, 1953.

This is an excellent introduction to color filters and the Munsell system of color value, hue, and chroma. While a medium green is recommended for civilian use, neutral gray glass has been developed for the Armed Forces to permit the most critical color discrimination. Other industrial protective glasses are described.

Paul W. Miles.

Stern, A. **The effect of target variation and kinesthesia upon near heterophoria measurements.** *Am. J. Optometry* 30:351-365, July, 1953.

Significant differences in measured heterophoria at 40 centimeters distance have been described in the prism diplopia test compared to various others. Differences are due to stimulus to "nearness" present in some tests, lack of necessity for accommodation due to size of object in others. Other tests involving simultaneous hand movements on the part of the subject to indicate phoria position produce significant changes toward esophoria. A target consisting of perspective clues in a picture of railroad tracks compared to a simple arrow or cross showed no significant variation.

Paul W. Miles.

Toselli, C. **The occurrence of aniseikonia in orthophoric emmetropes and isometropes.** *Boll. d'ocul.* 32:81-86, Feb., 1953.

Using the space eikonometer the author studied 100 persons aged between 10 and 62 years but mostly between 20 and 30. Excluded were anisometropes and persons with a horizontal phoria of more than two prism diopters and a vertical phoria of more than one. Forty-three of the 100 persons showed aniseikonia, total or meridional, never surpassing 1.5 percent. The lowest figure was 0.25 percent. Total aniseikonia was found in 13 persons, horizontal in 10 and vertical in 20. The smaller image was in the right eye of 17 and in the left of 26 persons. Repeated examination revealed the same error in the same person. No case of mixed aniseikonia was found. It is noteworthy that none of the aniseikonics complained of any of the symptoms often ascribed to this anomaly, such as photophobia, headache, or fatigue. (references)

K. W. Ascher.

5

DIAGNOSIS AND THERAPY

Brill, H. M., Long, J. S., Klawans, A. H., Golden, M., and Seaman, I. **The nitroglycerin flicker fusion threshold test in toxemia of pregnancy.** *Am. J. Obst. & Gynec.* 64:1201-1210, Dec., 1952.

The ordinary 60 Watt light bulb actually flickers 60 times per second, a rate of flicker that cannot be detected by the human eye. If this rate is reduced, it will be noted by every observer, usually when the flicker rate reaches about 40 per second. In reducing the flicker rate, the point at which flicker is detected by any individual, or the point at which flicker fuses into a steady source of light, is for that person, the fusion frequency threshold for flicker, or the F.F.T. The F.F.T. of each individual remains constant under given conditions unless it is changed by the use of drugs or the development of physical or pathological entities.

Usually, vasospasm is developed in the retina as an expression of a generalized disturbance. Such ocular vasospasm will interfere with vision and with the ability of the subject to detect flicker. If a patient is given 1/100 gr. nitroglycerin sublingually, the vascular spasm will be relieved, the ability to detect flicker will be improved, the fusion flicker threshold will be raised and the diagnosis of vasospasm becomes evident. This constitutes the Krasno-Ivy nitroglycerin F.F.T. test on which the present report is based, and the studies for which were made with the Krasno-Ivy flicker photometer.

The Krasno-Ivy flicker fusion threshold test is of value in the study of toxemia of pregnancy. By the use of this test it has been possible to predict the onset of toxemia in pregnancy before any clinical evidence of the disease becomes apparent. The test has permitted the evaluation of

the efficacy of treatment in toxemia of pregnancy. Cardiovascular-renal disease, pseudotoxemia, and toxemia have been differentiated through the use of this test.

Theodore M. Shapira.

Dorello, U., and Poli, L. **The ophthalmoscopic aspects of the fundus of the premature baby.** Arch. di ottal. 57:17-23, Jan.-Feb., 1953.

Forty-five premature babies of 2,500 gm. or less were examined on the tenth to the thirtieth day after birth. Three signs were observed which, however, can also be seen, though less frequently, in babies born at term: 1. pallor of the disc, 2. a grayish aspect of the periphery, and 3. particular accumulation of pigment in the posterior pole.

John J. Stern.

Marshall, M. F. P. **Infra-red image converter in rod scotometry.** Brit. J. Ophth. 37:316-317, May, 1953.

It is often of special advantage to be able to observe the eyes of a patient undergoing tests in the dark without affecting the dark adaptation of the test; this can be done with an infra-red image converter. An infra-red beam of light is directed at the patient's eyes and the observer watches through a fluorescent screen incorporated in an electronic device. The patient sees no beam of light but his eye movements are clearly seen.

Morris Kaplan.

Montgomery, John. **Integral implant following enucleation.** J. Tenn. St. M.A. 45:53-56, Feb., 1952.

The author describes his experiences with the newer artificial eye implants. In the majority of his cases, the new A.O. monoplex integrated implant is used. He believes in integral implants, for they give the patients far better movement and appearance. He feels that his results would have been better had he never used tan-

talum wire sutures and metals prongs. At present he uses silk or dermalon.

Theodore M. Shapira.

Ogle, K. N., and Rucker, C. W. **Fundus photographs in color using a high-speed flash tube in the Zeiss retinal camera.** A.M.A. Arch. Ophth. 49:435-437, April, 1953.

A modification of the camera is described in which a filament incandescent lamp replaces the carbon-arc lamp. The exposure of the tube is about 0.0001 second and therefore eliminates the problem of blinking and eye movements. Small details of the fundus are more satisfactorily photographed.

G. S. Tyner.

6

OCULAR MOTILITY

Urist, M. J. **Bilateral superior oblique paralysis.** A.M.A. Arch. Ophth. 49:382-391, April, 1953.

The author reports two cases of congenital bilateral superior oblique muscle paralysis in which the head tilt and presenting symptoms were those of a unilateral superior oblique palsy. Of practical interest is the fact that the bilaterality became apparent only after the more-involved inferior oblique muscle had been recessed surgically. After surgery on one inferior oblique, the patient developed head tilt to the opposite side from the original head tilt. The author proposes another explanation for the greater frequency of head tilt in superior oblique palsy than in superior rectus palsy.

G. S. Tyner.

7

CONJUNCTIVA, CORNEA, SCLERA

Cook, C., and Langham, M. **Corneal thickness in interstitial keratitis.** Brit. J. Ophth. 37:301-304, May, 1953.

In this study the correlation between

the corneal thickness and the rate of vascularization is recorded. In 10 cases of syphilitic and other keratitis, changes in thickness are watched in process of occurrence. In all cases the thickness of the cornea was directly related to the virulence of the keratitis and it was ascertained that corneal vascularization is always preceded by corneal edema. In all patients, the administration of cortisone subconjunctivally was followed by marked decrease in corneal thickness and then by a decrease in the associated infiltration and vascularization; corneal vascularization probably cannot occur without prior edema of the corneal tissue.

Morris Kaplan.

Recupero, E. **Serum iron levels in spring catarrh.** *Arch. di ottal.* 57:35-40, Jan.-Feb., 1953.

In nine children with spring catarrh, the iron content of the serum was lower than normal (66.4 gamma percent average compared with 100 gamma percent). This seems to indicate an increased need of the reticulo-endothelial system for iron and may explain the hypochromic anemia frequently encountered in the acute phase of spring catarrh.

J. J. Stern.

Strazzi, A. **Congenital heredo-familial corneal dystrophy.** *Riv. oto-neuro-oftal.* 27:307-318, July-Aug., 1952.

A case of corneal dystrophy is reported. The parents were first cousins; a daughter who died in infancy had the same eye disease. Corneal transplantation was performed twice in the right eye of the patient with final good result. The corneal material removed at the time of the first surgical intervention was studied histologically and revealed more or less large clumps of basophilic substance in the anterior region of the parenchyma. (3 figures, 10 references)

Bruno S. Priestley.

GLAUCOMA AND OCULAR TENSION

Dobree, J. H. **Vascular changes that occur during the phasic variations of tension in chronic glaucoma.** *Brit. J. Ophth.* 37:293-300, May, 1953.

That there must exist some relationship between intra-ocular tension and dilatation of episcleral vessels has long been suspected but only recently have methods of study been evolved to allow detailed examination of this possible relationship. In this study, variations throughout the day in caliber of episcleral veins, arteries and capillaries were recorded and compared to variations in ocular tension; this was done in chronic glaucoma simplex, in acute congestive glaucoma, and in normal eyes. The tests were made with minimal or no disturbance to the eye, frequently over a 24-hour period. In the low-tension glaucomas, the periods of greatest vascularity of the episcleral vessels was found to coincide in every case with the periods of lowest ocular tension; the veins only were affected. The greatest vascularity occurred between 8:00 p.m. and 6:00 a.m. Six of seven normal controls exhibited exactly the same variations in vascularity and this suggested that both the hypertension of the eye and the hypervascularity might well have the same physiologic cause. In the high-tension glaucomas the hypervascularity occurred largely in the periods of increased ocular tension; it was not necessarily bilateral and the arteries and veins were both affected. There must be some relationship between the diurnal variations in the vessel caliber and in ocular tension and further study might lead to more effective medical treatment of glaucoma.

Morris Kaplan.

Ferraris De Gaspare, P. F., and Maffei, G. **Audiometry in the provocative tests for the diagnosis of chronic glaucoma.**

Riv. oto-neuro-oftal. 26:294-326, July-Aug., 1951.

The authors used several of the usual provocative tests, for example, water drinking, caffeine, and dark room, in a series of 19 glaucomatous patients, with chronic, simple glaucoma, and then performed audiometric tests. Increased hypacusis followed in glaucomatous patients while in normal, arteriosclerotic, and presbycousic subjects the response was negative. The authors think that the audiogram is so characteristic that a diagnosis of glaucoma could be made by it alone, even without tonometric or visual field findings. (12 figures, 19 references)

Bruno S. Priestley.

Swan, K. C. **Miotic therapy of chronic glaucoma—changing trends.** A.M.A. Arch. Ophth. 49:419-430, April, 1953.

The basic pharmacology and physiology of miotic drugs are reviewed. Cholinergic drugs, such as pilocarpine, compete with cholinesterase-inhibiting drugs. Carbachol is a much more potent cholinergic drug than pilocarpine and may produce systemic effects from local application. To assure absorption, it should be used in a wetting agent or as a dry powder in an anhydrous base. Its use should be limited to pilocarpine-resistant patients. Eserine is seldom indicated in the routine treatment of chronic simple glaucoma because it acts as a chemical irritant. DFP is of value chiefly in aphakic eyes because its intense action on the ciliary body does not cause such marked visual disturbances in the absence of the lens. The action of DFP may be tempered when used in phakic eyes by prior instillation of pilocarpine. This effect is achieved because pilocarpine reduces the reactivity of the iris musculature. Similarly, the effect of pilocarpine may be enhanced by the occasional use of DFP.

G. S. Tyner.

10

CRYSTALLINE LENS

Bellows, J. G. **Lens and vitreous.** A.M.A. Arch. Ophth. 49:452-471, April, 1953.

The related literature is reviewed.

G. S. Tyner.

11

RETINA AND VITREOUS

Alper, M. G., and Alfano, J. A. **Honeycomb colloid degeneration of the retina.** A.M.A. Arch. Ophth. 49:392-399, April, 1953.

Seven cases of colloid degeneration of the retina in three generations of the same family are reported. Included in the report are an historical review, case histories, a pedigree of the family, visual fields, fundus drawings and photographs.

G. S. Tyner.

Ashton, Norman. **Arteriolar involvement in diabetic retinopathy.** Brit. J. Ophth. 37:282-292, May, 1953.

Extensive studies are being carried out in London's Institute of Ophthalmology on changes in the retinal arterioles in diabetes. It was determined that in the later stages of the disease the walls of the retinal arterioles are severely hyalinized and obliteration is responsible for a type of canalization within the retina and eventually for complete atrophy and destruction of the whole capillary bed. The retinas were removed in toto and the vessels injected with India ink which demonstrated the two aspects of the disturbance: 1. a narrowing or complete occlusion of the terminal arteriolar branches and precapillary arterioles, and 2. the formation of new channels on the venous side of the capillary network. The occlusion was generally found at the points of origin of the vessels and tended to progress with the severity of the diabetes.

The new channels were seen as dilated loops in the venous beds and generally followed the arteriolar obstruction. These changes are found only in the later stages of diabetic retinopathy and are not found in nondiabetic hypertensive or arteriosclerotic lesions. This may be a manifestation of exaggeration of ordinary sclerotic changes which are accepted as a complication of diabetes. These arteriolar changes could be the entire cause of the final destruction of the retina in severe diabetes.

Morris Kaplan.

Cross, A. G., and Choyce, D. P. **Unusual appearance in a case of Eales's disease.** *Brit. J. Ophth.* 37:314-315, May, 1953.

A 27-year-old man developed severe and recurrent bilateral vitreous bleeding during a presumptive tuberculosis of the eyes. The disease progressed despite all treatment and during the organization of the clots in one eye, the lens became dislocated backward and upward. The tension remained normal but extensive staphylomata resulted.

Morris Kaplan.

Jacobson, J., and O'Brien, J. M. **Electroretinographic studies in cases of pigmentary degeneration.** *A.M.A. Arch. Ophth.* 49:375-381, April, 1953.

24 patients with primary pigmentary degeneration of the retina were studied and the results tabulated. In all cases the electroretinogram showed a lack of response to the light stimulus. This lack of response was the same no matter in what stage the disease was found.

G. S. Tyner.

Lister, A. **Experiences with the Lindner-Guist operation.** *Brit. J. Ophth.* 37:305-311, May, 1953.

Some details of experiences with the Lindner-Guist operation for retinal detachment are recounted in honor of Lindner's seventieth birthday. The opera-

tion involves the use of potash as a corrosive agent rather than diathermy and is recommended when diathermy has failed to reattach the retina, or when the retina is generally atrophic and when the tears are at or near the macula. The technique recommended is to make a T incision through the sclera over the tear, exposing the choroid in a triangular area. The chemical, preferably a 3 percent potash solution, is injected and painted onto the choroid along the area of detachment. The subretinal fluid is then evacuated. In very severe cases, this is combined with scleral resection. The results have been encouraging.

Morris Kaplan.

Pascal, A. **Treatment of retinal detachment due to disinsertion at the ora serrata.** *Arch. di ottal.* 57:49-61, Jan.-Feb., 1953.

In twenty cases of detached retina with disinsertion, treatment with diathermic surface coagulation and puncture was successful.

John J. Stern.

12

OPTIC NERVE AND CHIASM

Streiff, M. E. B. **Trauma to the optic pathways.** *Riv. oto-neuro-oftal.* 26:356-390, Sept.-Oct., 1951.

The author reports numerous personal experiences with organic lesions of the optic pathway. He studies in detail the site of the lesions and the functional defects they cause. The diagnostic procedures are considered, including stereoradiography, behavior of the pupils, and visual fields. It is easier to localize a lesion when quadrantanopia is present. Hemianopia does not yield exact localization except when accompanied by other neurologic or otorhinologic signs. The importance of collaboration between ophthalmologist, neurologist, radiologist and otolaryngologist is emphasized. In trauma to the optic nerve (intracranial), unless there is improvement within the

first four days, decompression is warmly recommended. (22 figures, 138 references)

Bruno S. Priestley.

13

NEURO-OPHTHALMOLOGY

Anderson, J. R. **Causes and treatment of congenital eccentric nystagmus.** *Brit. J. Ophth.* 37:267-281, May, 1953.

Nystagmus may be divided into three groups by the types of movements; these are: 1. visual or fixation nystagmus, 2. oculomotor or gaze nystagmus, and 3. vestibular nystagmus. The causes of congenital nystagmus remain obscure. Congenital nystagmus owes its origin to a genetic, intra-uterine or birth factor and usually is not revealed until three or four months after birth. It is usually, but not necessarily, associated with reduced vision and presents a fast component to one side and a slow component to the other, with a minimum of movement at a point of rest. This point of rest is not always directly forward and when it is not, it results in head turning or tilting to make the point of rest straight ahead. In studying the causes of the condition, inheritance, maternal ill-health, types of labor and types of obstetrical analgesia were thoroughly considered. Inheritance and maternal health seemed to have little effect, while prolonged difficult labor resulting in fetal anoxia probably is the prime factor. Treatment should be recommended. Bilateral recession of the horizontal muscles to the side of the slow component, which is the opposite side to which the head is turned, results in bringing the position of rest directly forward and slows the fast component of the movement. In the four cases reviewed, satisfactory results were obtained.

Morris Kaplan.

Bartschi-Rochaix, W. **The test of optokinetic astasia in cases of cranial cere-**

bral trauma. *Riv. oto-neuro-oftal.* 26:391-398, Sept.-Oct., 1951.

This is an optokinetic test and is performed with the Barany drum. In 240 patients who had had head trauma a large number gave positive reactions, even a considerable time after the accident. The test should be of value in ruling out malingering.

Bruno S. Priestley.

Fasiani, G. M., and Beduschi, A. **Traumatic lesions of the intracranial optic pathway.** *Riv. oto-neuro-oftal.* 26:411-418, Sept.-Oct., 1951.

Seventeen cases of traumatic lesion of the third optic neuron are reported and classified according to the principles set by Belloni and Fasiani in 1940. In the present article the indications for early intervention are extended to the group of cases of amaurosis and amblyopia immediately following trauma.

Bruno S. Priestley.

Ghirardi, L., and Maione, M. **Arteriography of the ophthalmic artery especially in cases of intracranial hypertension.** *Riv. oto-neuro-oftal.* 26:426-437, Sept.-Oct., 1951.

In cerebral arteriography the ophthalmic artery is normally small, straight and visible only close to its origin and its branches are not visible. In cases of brain tumors or other lesions that may upset hemodynamic equilibrium of the cranial cavity the ophthalmic artery appears full, tortuous and all or nearly all of its branches become visible. (9 figures)

Bruno S. Priestley.

Otenasek, F. J., and Markham, J. **Transient loss of vision following cerebral arteriography.** *J. Neurosurg.* 9:547-551, Sept., 1952.

A case of transient visual failure following cerebral arteriography is described. Unilateral central scotoma on the injected side with constriction of peripheral fields

occurred within two hours after injection of 35-percent diodrast and recovery was complete within 48 hours. The possible mechanisms responsible for this reaction are discussed. Therapeutic stellate ganglion block with 1-percent procaine may have been beneficial. When impairment of vision occurs after cerebral arteriography and there is no ophthalmologic evidence of vascular alteration the prognosis for restoration of vision is probably favorable. Theodore M. Shapira.

Seidenari, Renato. **Optochiasmatic arachnoiditis with syndrome of Foster Kennedy.** Riv. oto-neuro-oftal. 26:438-444, Sept.-Oct., 1951.

The author describes a case in which there was optic nerve atrophy on one side and papilledema on the other. Tumor of the brain and of the olfactory groove were ruled out. The neurosurgeon found an extensive optochiasmatic arachnoiditis. (11 references) Bruno S. Priestley.

Walsh, F. B., and Smith, G. W. **Ocular complications of carotid angiography; the ocular signs of thrombosis of the internal carotid artery.** J. Neurosurg. 9:517-537, Sept., 1952.

The ocular symptomatology associated with the injection of diodrast into the common carotid artery are described. Seemingly the procedure holds an almost negligible threat as regards permanent loss of vision, and transient loss of vision occurs rarely. As far as the author is aware, no case of bilateral loss of vision has been seen as a result of angiography. He describes a remarkable case of transient bilateral homonymous hemianopsia. Thrombosis of the internal carotid artery is considered from the standpoint of its ocular symptoms and signs and several cases have been included to exemplify these manifestations. What seems an observation of importance occurred in five cases of hemianopsia. In all there was a tendency toward sparing of the upper

quadrant of the defective half-fields. From their studies of the arterial supply to the visual pathways it has seemed reasonable in these cases to assume that the principal arterial obstruction occurred in the branch or branches from the middle cerebral artery to the optic radiation. It seems unlikely that such a constant finding in the visual fields may have been merely the result of chance.

Theodore M. Shapira.

16

TUMORS

Pagliarini, N., and Cavicchi, L. **Ocular findings in malignant neoplasms.** Riv. oto-neuro-oftal. 27:273-287, July-Aug., 1952.

Five cases of metastatic choroidal tumors were observed, all originating from the breast. In two cases the affection was bilateral. Intractable glaucoma developed in one case which ended in enucleation. In the others Roentgen therapy and diathermy had a favorable influence on the ocular tumor. Therapy with male hormones slowed the process. A peculiar form of retinopathy similar to Roth's retinitis septica has been observed by other authors and called dysoric retinopathy, dysoria being an impairment of the blood-tissue barrier. In 200 cases the authors found this retinopathy only once. They could never find a retrobulbar neuritis. (17 references)

Bruno S. Priestley.

17

INJURIES

Franceschetti, A., Jentzer, A., and Maeder, G. **Post-traumatic ptosis of the eyeball and cure of diplopia by reconstruction of the orbital floor.** Riv. oto-neuro-oftal. 26:419-425, Sept.-Oct., 1951.

Fracture of the orbital floor is usually accompanied by ptosis of the globe, enophthalmos and diplopia. In the cases here reported, enophthalmos was not present but there was a most disturbing

diplopia, vertical as well as horizontal. Reconstruction of the orbital floor followed by orthoptic exercises brought back binocular single vision. (5 figures, 5 references)
Bruno S. Priestley.

Sabbadini, Dario. **Optic nerve severed in the optic canal. Late removal of bone splinter. Blindness.** Riv. oto-neuro-oftal. 26:399-403, Sept.-Oct., 1951.

A fall from an airplane had caused the patient to hit his frontal region violently against the ground. The left eyeball was ruptured, the right had no light perception. Ophthalmoscopy showed commotio retinae in the right eye. The disc appeared to be normal. X-ray with Busi's projection revealed a bony splinter occupying the optic foramen. The splinter had severed the optic nerve. Surgery had to be delayed because of meningitis, but the author is convinced that even earlier intervention could not have saved the eyesight in this case. (1 figure)

Bruno S. Priestley.

18

SYSTEMIC DISEASE AND PARASITES

Magni, Sallustio. **Behcet's disease with meningo-encephalitic complications.** Riv. oto-neuro-oftal. 26:445-452, Sept.-Oct., 1951.

A patient with Behcet's disease had numerous attacks of anterior uveitis with hypopyon, periphlebitis retinae as well as affections of the mucous membrane and skin. After five years, disturbance of the central nervous system became manifest. Three years later he died and autopsy showed a meningo-encephalitis. No definite etiology could be found but the author believes that the cause was a virus infection.

Bruno S. Priestley.

Magni, S. **Ocular mucocutaneous syndromes.** Riv. oto-neuro-oftal. 27:288-306, July-Aug., 1952.

The author discusses three diseases: Stevens-Johnson's disease, Reiter's dis-

ease and Behcet's disease. He is opposed to the unitarian interpretation that considers them all as manifestations of one fundamental disease, namely multiform exudative erythema. (42 references)

Bruno S. Priestley.

19

CONGENITAL DEFORMITIES, HEREDITY

Cima, V. **Pupillary reflex in monozygous twins.** Riv. oto-neuro-oftal. 26:287-293, July-Aug., 1951.

In three pairs of monozygous twins, the behaviour of pupillary reactions, size of pupils and pupillograms proved different in each twin. (4 figures, 16 references)

Bruno S. Priestley.

Falls, H. F. **Albinism.** Tr. Am. Acad. Ophth. 57:324-331, May-June, 1953.

The ocular aspects of albinism are reviewed. It has been suggested that the clinical picture (phenotype) exhibits a rather wide range of variability. This is substantiated by the appearance of many different hereditary patterns (genotypes). Sorsby's classification has been presented in modification. The oculist is advised to anticipate albinism as a possible etiologic agent in photophobia, nystagmus, high errors of refraction, head nodding and reduced visual acuity. It is suggested that most of the signs and symptoms of albinism improve with advancing age and with the accumulation of pigmentation. Encouraging therapeutic advances in albinism seem probable in the not too distant future.

Theodore M. Shapira.

Rizzo, Paolo. **The syndromes characterized by microphthalmos and limbus malformation.** Riv. oto-neuro-oftal. 26:327-334, July-Aug., 1951.

The author describes a case of microphthalmos with malformation of the limbus which closely resembles Biemond's syndrome. (2 figures, 21 references)

Bruno S. Priestley.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month, but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received at least three months before the date of occurrence.

DEATHS

Dr. Royal Jackson Calcote, Little Rock, Arkansas, died June 28, 1953, aged 59 years.

Dr. Fay Maxey Cooper, Oklahoma City, Oklahoma, died June 16, 1953, aged 53 years.

ANNOUNCEMENT

ESTELLE DOHENY LECTURE

The fourth Estelle Doheny Eye Foundation Lecture will be delivered on Thursday evening, November 5th, at eight o'clock in the Los Angeles County Medical Association Building. Dr. Frederick C. Cordes, clinical professor of ophthalmology at the University of California School of Medicine, San Francisco, will deliver this lecture. His subject will be "Endocrine exophthalmos: An evaluation."

SOCIETIES

EAST BAY SOCIETY

Dr. Jay Sharpsteen has been elected president, and Dr. Ernest E. Hessing, secretary, of the Ophthalmological Society of East Bay, Oakland, California. Dr. Hessing's address is 483-30th Street, Oakland 9, California.

MISCELLANEOUS

EYE-BANK AFFILIATE

The board of directors of the North Carolina Eye-Bank are requesting affiliation with the parent and original eye-bank, The Eye-Bank for Sight Restoration, Inc., of New York City.

SYRACUSE POSTGRADUATE COURSE

The Department of Ophthalmology of the State University of New York Medical Center at Syracuse will present its fourth annual postgraduate course in ophthalmology at the Hotel Syracuse, Friday and Saturday, December 11th and 12th.

Guest lecturers who will participate are: Dr. Alan C. Woods, Dr. Harold Falls, Dr. Hunter H. Romaine, and Dr. Franklin M. Foote.

The tuition fee will be \$25.00 payable to the State University of New York Medical Center at Syracuse, Irving Avenue, Syracuse, New York. This fee covers tuition, daily luncheons, and dinner Friday night. The course will be limited to 60 members. These will be accepted in the order in which applications accompanied by checks are received. Inquiries regarding the course may be addressed to Dr. Harold H. Joy, 504 State Tower Building, Syracuse, New York.

YALE POSTGRADUATE SERIES

The Yale University School of Medicine Postgraduate Series in Ophthalmology opened on October 9th with a case presentation by Dr. Eugene M. Blake on "The treatment of acute congestive glaucoma." On October 14th, Dr. David G. Cogan presented a paper on "Ophthalmic manifestations

in the neurologic patient."

The series will continue through May 28, 1954, with the following program scheduled:

November 13th, a case presentation by Dr. J. Miles O'Brien, Bridgeport, Connecticut, on "Electroretinography."

November 20th, "Aides in the diagnosis of glaucoma," Dr. Willis S. Knighton, New York.

December 11th, case presentation by Dr. Robert C. Good, Waterbury, Connecticut.

January 8th, 1954, case presentations by Dr. Arthur C. Unsworth and Dr. Chester A. Weed, Hartford.

January 29th, Dr. Alfred Cowan, Philadelphia, will discuss "Refraction problems: Questions and answers."

February 12th, "Experimental studies on exophthalmos," Dr. George K. Smelser, New York, and case presentations.

February 26th, Dr. Arthur Gerard DeVoe, New York, "An evaluation of the plastic procedures available to the ophthalmic surgeon."

March 12th, case presentations and a paper by Dr. Leon S. Stone, New Haven, on "Eye embryologic defects."

March 26th, "The eye in symbol and symptom," Dr. Henry H. Hart, New York.

April 9th, "Suprachoroidal iridencleisis," Dr. Francis P. Guida, New Haven.

April 30th, "The method of concordance in the diagnosis of strabismus," Dr. Joseph I. Pascal, New York.

May 14th, "The management of industrial ocular problems," Dr. Arthur M. Yudkin, New Haven.

May 28th, Dr. Conrad Berens, New York, will discuss "Uveitis."

The dues for this postgraduate series are \$15.00, payable to Dr. Frederick E. Mott, treasurer, 38 Trumbull Street, New Haven, Connecticut. Dr. Rocko M. Fasanella, head, Section of Ophthalmology, Yale University School of Medicine, is chairman of the series.

SEMINAR ON NEURO-OPHTHALMOLOGY

The third year of a seminar meeting in about 10 sessions on the first Friday of each month, beginning in October, is announced by the Yale University School of Medicine. The meetings will take place at 10:30 A.M. in Room 2020 of Farnam Memorial Building.

FLORIDA MIDWINTER SEMINAR

The eighth annual University of Florida midwinter seminar in ophthalmology and otolaryngology will be held January 18 through 23, 1954, at Miami Beach at the San Souci Hotel. In charge of the Division of Ophthalmology are Dr. Shaler Richardson, Jacksonville; Dr. Nelson M. Black, Miami; Dr. Charles W. Boyd, Jacksonville; and Dr. Bascom H. Palmer, Miami.

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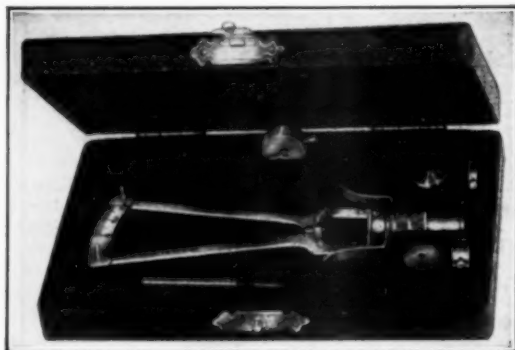
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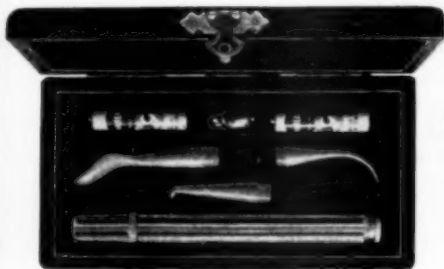


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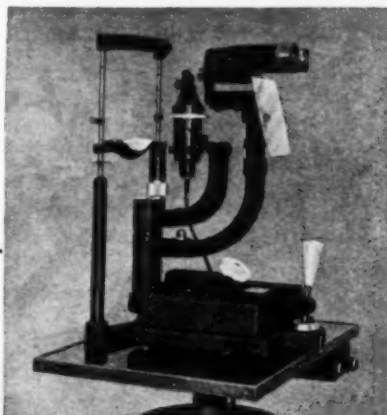
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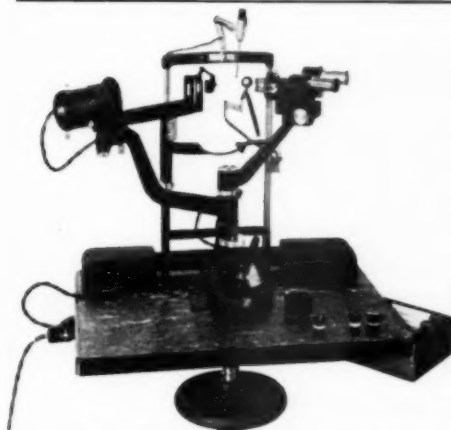
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